EXPLICIT DEFINITIONS TO IDENTIFY PREVENTABLE DRUG-RELATED MORBIDITY IN AN ELDERLY POPULATION AND THEIR USE AS AN INDICATOR OF QUALITY IN THE MEDICATION USE SYSTEM

By

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This dissertation is dedicated to my lovely wife, Leanne and wonderful son Seth. Thank you for your love, support and acceptance, regardless of the circumstances.

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TABLE OF CONTENTS

Abstract of Dissertation Presented to the Graduate School
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Requirements for the Degree of Doctor of Philosophy

EXPLICIT DEFINITIONS TO IDENTIFY PREVENTABLE DRUG-RELATED MORBIDITY IN AN ELDERLY POPULATION AND THEIR USE AS AN INDICATOR OF QUALITY IN THE MEDICATION USE SYSTEM

By

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Major Department: Pharmacy Health Care Administration

This study was undertaken to develop explicit definitions of preventable drug-related morbidity (PDRM), and use these definitions to measure PDRM in an elderly managed care population. The Delphi technique was used with a geriatric medicine expert panel to come to consensus on 49 explicit definitions of PDRM in the elderly. These definitions were then operationalized using ICD-9, CPT and NDC codes that were compatible with a managed care organization's database of patient information. There were 11,711 patients eligible for the study. The explicit definitions detected at least one instance of preventable drug-related morbidity in 8.2% (966) of eligible patients. A rate of 6.25 events per 100 patient years was detected.

Evidence for validity of the definitions was gathered through the use of known risk factors and health care resource use. The presence of PDRM was significantly associated with the number of prescriptions a patient received, the number of diagnoses, the number of prescribers, and patients over 85. Patients with a preventable drug-related

morbidity event detected also used significantly more health care resources and cost more to care for than those without an event. The resource use included hospitalizations, emergency room visits, physician office visits and medications.

The measure of preventable drug-related morbidity was used as part of a quality assessment and improvement exercise to demonstrate its utility in uncovering quality problems in the medication use system. An expert panel generated four cause-and-effect diagrams that could be used to structure improvement opportunities. Thus, the measure was useful in a formative system.

This study is important in its development of explicit definitions for PDRM and linking the presence of the pattern of care with the corresponding adverse outcome. These definitions may be used as indicators to measure and monitor the performance of the medication use system. Ultimately, they may be used to monitor the pharmaceutical care of individual patients.

CHAPTER 1
INTRODUCTION

The Need for the Study

Medications are the most common treatment prescribed in health care. The majority of patients who visit the doctor's office leave with a prescription (Schappert, 1994). However, the act of writing a prescription does not assure optimal outcomes.

Medication use requires several steps to achieve the desired outcome. These steps appear fragmented in today's health care environment. The result is a medication use process that is unsafe. Problems stem from systematic flaws in the process, poor communication among participants in the system, the lack of defined therapeutic objectives, and inadequate feedback mechanisms needed for systems improvement (Grainger-Rousseau et al., 1997; Schaff et al., 1991).

A process of poor quality will often produce poor outcomes. In terms of medication use, a poorly functioning process leads to patients receiving sub-optimal drug therapy. Sub-optimal drug therapy may lead to patient injury (drug-related morbidity) or death (drug-related mortality). Patient injury and death impact both patients and society. Studies have shown that patient death from medication use is an important issue that must be addressed (Institute of Medicine Committee on Quality Health Care in America, 1999; Lazarou et al., 1998; Talley & Laventurier, 1974).

Drug-related morbidity (DRM) may reduce a patient's quality of life and ability to function in society. It may also impact the patient financially through direct medical expenses (i.e., co-pays and deductibles), indirect medical expenses, and lost productivity.

The financial impact of drug-related morbidity and mortality on society is enormous. Johnson and Bootman (1995) estimated that drug-related morbidity and mortality in ambulatory care patients cost society $76 billion dollars each year. This estimate would place it among the most expensive "disease states" and most important patient safety issues in health care.

Direct health care resources used to treat drug-related morbidity are substantial. Care in a hospital setting is expensive and is often used to treat the consequences of DRM (Bergman & Wiholm, 1981; Bero et al., 1991; Bigby et al., 1987; Caranasos et al., 1974; Hallas et al., 1992; Lakshmanan et al., 1986; Lindley et al., 1992; Nelson & Talbert, 1996). Studies suggest that up to 20% of all hospital admissions are drug-related (Bergman et al., 1981; Bero et al., 1991; Bigby et al., 1987; Caranasos et al., 1974; Cunningham et al., 1997; Hallas et al., 1992; Lakshmanan et al., 1986; Lindley et al., 1992; Nelson & Talbert, 1996).

Other health care products and services such as the emergency room, physician office visits, long-term care, skilled nursing care, and medications are used to treat DRM (Bootman et al., 1997; Dennehy et al., 1996; Hanlon et al., 2000; Johnson & Bootman, 1995; Rossiter et al., 2000). The lost opportunity costs for the health care system are substantial.

As stated above, drug-related morbidity is a problem in the medication use system that reduces the quality of care received by patients and increases the total cost of health care. Like any epidemic, prevention is the most efficient and humane strategy. The idea of preventability is gaining momentum in the literature. Research suggests that around 50% of DRM events are preventable (Bates et al., 1995b; Bates et al., 1993; Bigby et al.,

1987; Culler et al., 1998; Dubois & Brook, 1988; Hallas et al., 1990; Nelson & Talbert, 1996). Preventing drug-related morbidity would significantly improve the safety and quality of the medical care system, while at the same time reducing average per-patient cost.

Despite the increased attention preventability has received, there is no consensus in the literature either defining or measuring its prevalence (Ross, 2001). Because there is no consistent method for identifying and reporting instances of preventable drug-related morbidity, research results show wide variability in terms of the rate of events and their preventability.

Current efforts to identify and evaluate drug-related events usually include intensive surveillance and chart review. Implicit review methods are often labor intensive, expensive, and difficult to replicate (Brennan, 2000; Donabedian, 1978). In addition, many published studies look only at patients in the hospital setting or their reason for admission. By focusing on acute care settings, many problems are left undiscovered (Karch & Lasagna, 1975). More effort needs to be directed at the entire continuum of care, specifically ambulatory care.

Improved methods of identifying and measuring drug-related morbidity are needed to maximize efforts focused on preventing these events. Emerging computer technology provides a new opportunity for surveillance and identification of drug-related morbidity (Maass & Cortezzo, 2000; Raschke et al., 1998). The use of computers will facilitate the surveillance of large populations of patients across care sites. This may be accomplished by developing explicit criteria and applying them to computerized patient information as an indicator of potential quality problems. Computer screening with

explicit criteria will provide more complete information, speed up data review, and reduce the costs associated with measurement. Thus, explicit criteria to measure preventable drug-related morbidity will add valuable information to improve the quality of medication use across organizations.

Problem Statement

The medication use system currently in place is fragmented and lacks feedback necessary for improvement. This results in medication use that is not optimal and may lead to patient injury. Drug-related injury is a problem for patients and the health care system. Patients may experience a reduced quality of life or even death as a result of the improper use of medications. Meanwhile, the health care system is spending billions of dollars treating patients with drug-related morbidity and mortality (Johnson & Bootman, 1995; Thomas et al., 1999). The literature suggests that about 50% of DRM is preventable (Bates et al., 1995b; Bates et al., 1993; Bigby et al., 1987; Culler et al., 1998; Hallas et al., 1990; Nelson & Talbert, 1996). Preventing drug-related morbidity will result in substantial savings for the health care system and improve the quality of life for patients.

The measurement of preventable drug-related morbidity is hindered by the lack of consensus regarding terminology and reliable methodologies (Ross, 2001). The health care literature currently appears to support expert review to determine rates of DRM. However, implicit review by experts is difficult to replicate and would be cost prohibitive in most organizations. Because of the lack of widespread measurement, many leaders of health care organizations may be unaware that preventable drug-related morbidity (PDRM) is a problem. Without recognizing PDRM as a significant safety and financial issue, resources will not be directed at correcting a faulty medication use system.

A recent report by the Institute of Medicine (1999) recommends the development and testing of indicators to track medication errors and to develop preventative strategies based on the results. Explicit definitions for PDRM may serve this purpose. Explicit criteria to measure PDRM are now possible with advancing computer technology. MacKinnon (1999) has defined specific scenarios of PDRM that could be used as explicit measures of PDRM and as an indicator of the quality of the medication use system. This work will lead to more efficient methods of determining the prevalence of PDRM and bring much needed attention to the issue.

Study Objectives

There are four objectives in this study:

1. To develop explicit definitions of preventable drug-related morbidity,
2. To identify issues in operationalizing the definitions of PDRM to be used in a computer database,
3. To measure preventable drug-related morbidity in an elderly managed care population, and
4. To use the measure of preventable drug-related morbidity in a structured quality assessment and improvement framework to identify quality problems.

Research Questions

To accomplish the objectives of this study, several research questions will be investigated.

Research Question 1

Can the definitions developed by MacKinnon (1999) be face and content validated in a different physician panel?

Research Question 2

What issues are involved in operationalizing definitions of preventable drug-related morbidity for use in a computer database?

Research Question 3

Can PDRM be measured in an existing computer database?

Research Question 4

What is the prevalence of PDRM in an elderly Medicare population?

Research Question 5

Are there risk factors that are more common in patients with preventable-drug related morbidity?

Research Question 6

What is the relationship between patients with PDRM and their utilization of health care resources?

Research Question 7

Can a measure of PDRM be used to identify breakdowns in quality in the medication use system?

CHAPTER 2
REVIEW OF LITERATURE AND FRAMEWORK

Medication Use

Technological advances in the diagnosis and treatment of medical conditions continue at unparalleled levels (Mootonen et al., 2001). The information and resources available to health care practitioners today were unheard of just a few decades ago. One area of health care that has grown exponentially in the latter half of the twentieth century, in both knowledge and available options, is medication therapy.

Today, medications are the most common treatment modality used in the United States (Schappert, 1994). Approximately 63 percent of all physician office visits result in a written prescription (Schappert, 1994). Medications are an important component of patient wellness. The Joint Commission on the Accreditation of Healthcare Organizations (JCAHO) promotes the appropriate, safe, effective, and efficient use of medications as a necessary clinical function to assure positive patient outcomes (Schaff et al., 1991).

As a legitimate therapeutic alternative, there are four objectives of drug therapy; (1) cure a disease, (2) reduce or eliminate symptoms of a disease, (3) arrest or slow the disease process, and (4) prevent the disease or symptoms (Hepler & Strand, 1990). However, the act of prescribing a medication does not assure optimal outcomes. The medication use process is a series of steps that must operate together to attain the intended outcome. It is the complexity and number of steps in the medication use process that increase the likelihood of an adverse outcome (Leape, 1994).

Each year, an estimated 1.3 million persons are injured as a result of the medical care they receive (Cullen et al., 1997). Medications have been implicated as the leading cause of injuries due to medical care (Brennan et al., 1991; Leape et al., 1991). Thus, despite the advances in technology, education and training of health care practitioners, and the availability of newer and presumably safer drug entities, evidence suggests that patients are placed at risk when they are prescribed medications for legitimate therapeutic reasons and follow advice given by health care professionals.

Impact of Drug-Related Morbidity

We will examine three issues as they relate to drug-related morbidity; 1) how much it costs, 2) the impact on the quality of care, and 3) the impact on patient access to services.

Cost

Drug-related morbidity is a burden for society in terms of direct health care expenses. Johnson and Bootman (1995) estimated that drug-related morbidity and mortality cost society $76 billion dollars a year (1995 dollars). This amount would place drug-related morbidity and mortality among the most expensive disease states.

Several studies have examined the impact of drug-related morbidity on hospital admissions. Studies suggest that up to 20% of all hospital admissions are drug-related (Bergman & Wiholm, 1981; Bero et al., 1991; Bigby et al., 1987; Caranasos et al., 1974; Cunningham et al., 1997; Hallas et al., 1992; Lakshmanan et al., 1986; Lindley et al., 1992; Nelson & Talbert, 1996). Hospital costs were expected to reach $518 billion in the year 2000 (Burner & Waldo, 1995). Thus, drug-related hospital admissions could cost $103 billion, or approximately 7% of estimated total health care expenditures in 2000 (Burner & Waldo, 1995).

Drug-related morbidity occurring in hospitalized patients affects both cost and quality. Studies have demonstrated that patients who experience an adverse drug event (ADE) in the hospital cost significantly more to care for and had a longer length of stay. (Bates et al., 1997; Classen et al., 1999; Geraci et al., 1999; Pearson et al., 1994; Schimmel, 1964; Weingart et al., 2000).

Drug-related morbidity can increase the number of emergency room visits, unscheduled physician office visits, nursing home admissions, and the cost of medications a patient is taking (Bootman et al., 1997; Dennehy et al., 1996; Hanlon et al., 2000; Johnson & Bootman, 1995; Rossiter et al., 2000). When added together, the total direct heath care expenditures to treat drug-related morbidity should demand attention.

Quality

Drug-related deaths may be the most alarming quality issue in health care today. The 1999 Institute of Medicine report estimates that approximately 98,000 patients die each year from preventable medical errors (Institute of Medicine Committee on Quality Health Care in America, 1999). This report generated debate on the issue, expanding beyond the medical community. Politicians have pledged additional dollars to study and reduce these events. However, what is new to the politicians is not new to the health care system.

In 1974, Talley and Laventurier estimated that up to 140,000 deaths each year were caused by adverse drug reactions. Lazarou et al. (1998) performed a meta-analysis of past adverse drug reaction studies and estimated that 4.6% of recorded deaths in the United States were due to adverse drug reactions. This result would place adverse drug reactions between the 4^{th} to 6^{th} leading cause of death in this country. These figures

warrant investigation into medication use and methods for reducing drug-related injury and death.

Access

Many persons in the United States have limited access to health care (Culler et al., 1998). This limited access may be due to inadequate health insurance, the high cost of seeking care without insurance, or the lack of physical facilities or health care professionals within reasonable travelling distance.

Drug-related morbidity is increased when access to medical care is limited. Culler et al. (1998) state

> access to timely and effective ambulatory medical care may reduce the risk of hospitalization for selected medical conditions either by preventing the onset of disease, by controlling an acute episodic illness or condition, or by managing a chronic disease or condition in such a way as to prevent progression of the disease. (p. 804)

Patients who do not seek care when they have a medical indication will not receive the necessary treatment and monitoring to alleviate symptoms or cure their disease. Eventually, the patient's condition may deteriorate and require additional health care services.

Access can be further impacted by a patient's attitude towards past care. If patients are dissatisfied with the care they receive, they may be less willing to access the health care system in the future (Gandhi et al., 2000).

Preventability of Drug-Related Morbidity

As with any medical problem, prevention is the most humane strategy. Formerly, the preventability of adverse events due to medication use went largely unrecognized. In 1955, Barr stated that adverse drug reactions were the "price we pay" for using these chemical agents. Moser (1956) added to this sentiment by stating that adverse drug

reactions were a "disease of medical progress." In essence, they were saying that we must accept the risk because the benefits outweigh any harm. While these statements were made in the 1950's, they seem to reflect the thought on the subject for many years since then. This prevailing thought is illustrated in a recent article by Lazarou et al. (1998) where the authors seem to lament the perceived lack of preventability of adverse drug reactions.

The idea of preventability had not received a lot of attention prior to 1970. Melmon (1971) was one of the early authors that addressed preventability. Melmon (1971) stated that 70-80% of drug reactions were predictable. If these events were predictable, prevention is possible. Melmon (1971) further debunked the idea that adverse effects were a "disease of medical progress" by stating these events were preventable "without compromise of the therapeutic benefits of the drug" (p. 1366). Melmon (1971) went on to recommend possible causes of adverse drug reactions and what might be done to reduce their incidence and impact.

Studies now indicate that around 50% of drug-related morbidity are preventable (Bates et al., 1995b; Bates et al., 1993; Bigby et al., 1987; Culler et al., 1998; Dubois & Brook, 1988; Hallas et al., 1990; Hallas et al., 1992; Johnson & Bootman, 1995; Lakshmanan et al., 1986; Nelson & Talbert, 1996). If 50% of drug-related morbidity can be prevented, significant gains in the quality of care and reductions in costs are possible. Preventing half of Johnson and Bootman's (1995) cost-of-illness estimate would yield savings of $38 billion each year. The impact of prevention cannot be understated. However, in order to prevent these events, it is necessary to understand quality assessment and improvement techniques and the system of medication use.

Quality Assessment and Improvement

Quality assessment and improvement programs have been popular in health care since the late 1980's. These programs take many different names such as continuous quality improvement (CQI), total quality management (TQM), performance improvement (PI), or quality improvement (QI). However, their basic premise is the same: to look at the system of care in place, measure the current level of function, identify and implement improvement opportunities, and re-measure the system to determine the impact of the changes. One framework commonly used in health care to organize the process is referred to by the acronym FOCUS-PDCA. The Columbia/HCA Corporation (Nashville, Tennessee) developed the FOCUS-PDCA process as an extension of the PDCA cycle (Gerard & Arnold, 1996). The following steps are proposed as a systematic process for quality assessment and improvement:

- **F**ind a process to improve.
- **O**rganize a team that understands the process.
- **C**larify current knowledge of the system.
- **U**nderstand the causes of variation.
- **S**elect the improvement or intervention.
- **P**lan the improvement.
- **D**o implement the improvement.
- **C**heck the improvement by gathering and analyzing data.
- **A**ct on the data to hold the gain or continue improving.

Within each step of the FOCUS-PDCA process, there are "tools" available to uncover quality problems and guide the identification of improvement opportunities.

Some of these tools include the flow chart, run charts, control charts, Pareto charts and root cause analysis.

The theory of quality assessment and improvement (and the FOCUS-PDCA process) fits well with the idea of preventing drug-related morbidity. By using quality assessment and improvement techniques, flaws in the medication use process, which cause PDRM, are uncovered and changed with lasting results. This will require a measure of PDRM that can serve as a valid indicator of improvement opportunities.

An indicator is a tool used to monitor and evaluate the quality of important governance, management, clinical, and support functions that affect patient outcomes (Angaran, 1991). Indicators are used as screens to detect potential problems in the quality of care. Indicators selected should tap key areas of the medication use system. Many quality assessment and improvement programs operate by looking at the structure, process, and outcomes of our systems (Donabedian, 1978). To examine medication use and why indicators of quality problems may be beneficial, a review of structure, process and outcome is warranted.

Structure, Process and Outcome

Structure refers to the material and social instrumentalities that are used to provide care (Donabedian, 1978). These may include the physical environment, the training and qualifications of the personnel, and organizational issues. The structure component of the medication use system has received a lot of attention in past years due to efforts by the Joint Commission on Accreditation of Healthcare Organizations (JCAHO), state boards of pharmacy, and others.

The process and outcome components of quality are currently receiving the majority of attention in health care. Process refers to those steps or procedures used to

carry out the care of patients. Processes of care are important insomuch as they lead to the desired outcome (Donabedian, 1978). Outcomes are defined as the change in health status that can be attributed to the care provided (Donabedian, 1978).

A poor medication use process can reduce the quality of care by placing a patient at risk for additional harm (i.e., poor outcomes). This risk can manifest itself as further medical conditions, a worsening of symptoms, a reduction in the patient's quality of life, or even death. Thus, it is important to identify key measures (indicators) of the medication use process that may reflect quality problems. Once key indicators are in place, then tools such as root cause analysis are used to determine where the breakdowns occur.

Root Cause Analysis

Root cause analysis has been used as a quality assessment and improvement tool in health care (Fernandes et al., 1997; JCAHO, 1996; Shinn, 2000). Root cause analysis (RCA) is a method that uncovers the causes of quality problems and the relationship between the cause and the net effect (JCAHO, 1996). It is important to note that root cause analysis does not establish the magnitude of the individual causes identified. The results of a root cause analysis lack both time and quantitative data. Additional quality assessment and improvement tools are needed to determine which quality issues are most important.

A root cause analysis allows participants in a problem solving process to utilize information gathered to reason out possible causes for poor quality (Shinn, 2000). From this reasoning process, system changes are identified and implemented. Thus, the medication use process is amenable to a root cause analysis.

The Medication Use System

The medication use system has not changed appreciably in many years. However, the demands on the system have changed dramatically due to an increase in technology and the availability of treatment options (Mootonen et al., 2001). The medication use process has become very complex and fragmented in nature (Leape et al., 2000). There are many opportunities for breakdowns in the system when components of the process operate independently. The lack of communication among the doctor, patient, pharmacist, and others involved in patient care further reduces the quality and safety of medication use (Bates, 2000).

The current medication use model for prescription medications is detailed in Figure 2.1 (emphasis added at the end) (Nadzam, 1998). In ambulatory care, this process begins with a physician office visit that culminates in a prescription being written. The patient is then responsible to have the prescription filled at a pharmacy. At that point, the patient is responsible to take the medication and monitor results.

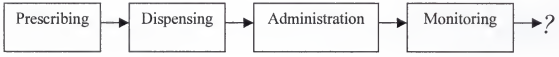


Figure 2.1: Current Medication Use Process (Nadzam, 1998)

As suggested in the medication use model, no consistent feedback mechanism exists to detect and correct drug-related problems. The assumption appears to be that once the medication is prescribed correctly and dispensed properly, optimal outcomes are assured. Thus, the last step in the process is truly the end until another office visit or drug-related morbidity occurs.

Given the limitations of the current medication use process, there is a need to redesign the system to foster the prevention of adverse events. Hepler and Grainger-Rousseau (1995) have proposed a medication use system that links the steps of the process and includes an integrated monitoring plan directed at detecting and resolving drug-related problems (See Figure 2.2). The addition of an explicit feedback mechanism changes the process into a system.

As medication use is viewed as a system, quality assessment and improvement activities can have their greatest impact. The outcomes by which success is judged will become more obvious as quality assessment and improvement become the standard. A system that identifies goals at the beginning of therapy will set in place a monitoring strategy with indicators designed to detect success or failure. This monitoring system will include the detection and resolution of drug-related problems as they arise.

Defining and Measuring Drug-Related Morbidity

Patient injury as a consequence of drug therapy is a popular topic in the literature. Over the last few decades, many attempts to define drug-related events and assess their preventability have been made. Despite these efforts, no clear consensus exists and there is much confusion regarding terminology (Ross, 2001). A review of the terminology follows.

Adverse Drug Reactions

The most widely recognized and measured adverse event involving drug therapy is an adverse drug reaction (ADR). In 1970, the World Health Organization (WHO) defined an adverse drug reaction as

> any response that is noxious, unintended, and undesired and that occurs at doses normally used in man for prophylaxis, diagnosis, or therapy. (p. 103)

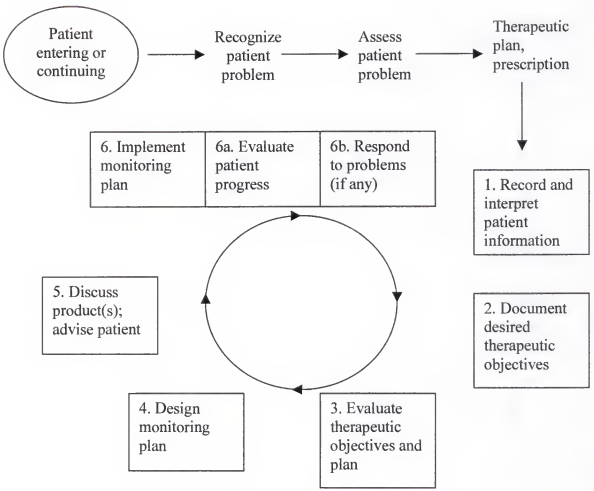


Figure 2.2: Medication Use System (Hepler & Grainger-Rousseau, 1995, p. 6)

Despite its wide use in the literature, the World Health Organization's definition of an ADR has limitations. There are differing opinions on whether the definition includes the failure to accomplish the intended purpose (drug therapy failure). Bergman and Wilholm (1981) believe the failure to accomplish the goal is not included. Meanwhile, Karch and Lasagna (1975) state that the definition could be interpreted to include this classification, but recommend it not be. They base this recommendation on their interpretation that the failure of a drug to produce a desired effect is qualitatively different than the production of an undesirable effect. This position appears somewhat irrational as the failure to produce the desired effect is by definition undesired.

The definition of an adverse drug reaction would also call into question efforts to prevent occurrences since they are unexpected and occur at therapeutic doses (Lazarou et al., 1998; Ross, 2001). Preventability did not receive much, if any, attention in the early stages of defining and identifying adverse drug reactions (Karch & Lasagna, 1975).

Preventability of adverse drug reactions is further hindered by the excessive focus on linking a specific drug entity to the adverse event. This is best illustrated by the algorithms developed to assist in identifying the causative agent (Kramer et al., 1979; Naranjo et al., 1981). Focusing on the drug as the primary cause (rather than the use of the drug) hinders efforts to uncover problems in the medication use system. Thus, without a systems perspective, improvement activities using ADR information are limited.

Some researchers have addressed the preventability of ADRs. Hallas et al. (1990) looked at consecutive admissions to assess drug-related hospitalizations. They used the term avoidability rather than preventability. Their study classified events as definitely

avoidable, possibly avoidable, not avoidable, or unevaluable. A definitely avoidable event was one in which

> the drug event was due to a drug treatment procedure inconsistent with present-day knowledge of good medical practice or was clearly unrealistic, taking the known circumstances into account. (Hallas et al., 1990, p. 85)

Hallas et al. (1990) used an implicit format for evaluating the causative nature of a hospital admission and its avoidability. Avoidability was assessed only in events judged to have been definite or probable in their causal relationship with the drug, and where the symptoms played a role in the hospital admission. Their use of present-day knowledge in evaluating avoidability gives the appearance of evidence-based criteria. However, the use of physician review may open the door for local practice standards to override evidence.

Hallas et al. (1990) advocate an intensive monitoring program by suggesting that a valid estimate of drug-related hospitalizations will only be obtained if a qualified individual evaluates each case independently. However, this may not be practical or possible in most organizations.

Medication Errors

Medication errors are receiving more attention in both the peer-review and lay press. A report released by the Institute of Medicine (IOM) in 1999 caused politicians, health care professionals, and the public to intensify the search for answers to this problem (Institute of Medicine Committee on Quality Health Care in America, 1999).

Health care professionals have been addressing the issue of medication errors for some time. In fact, entire books have been published on the issue (Cohen, 1999). A medication error has been defined as "an error in the process of ordering or delivering a medication" (Cullen et al., 1995, p. 543). In ambulatory patients, this could be

interpreted as the prescribing or dispensing of medications. In the institutional setting, this would also include the administration of the drug. However, neither covers the entire medication use system described previously.

Labeling an event a "medication error" may lead to a misdirected search for causes. When an event is referred to as an error, fixing of blame (or finding fault) on individuals often follows (Berwick & Leape, 1999; Reinersten, 2000). Reinersten (2000) supports this by stating, "deep down we believe that individual diligence should prevent error" (p. 730). Disciplinary action against the individual(s) identified in the investigation is often the remedy applied to fix the problem. By blaming individuals for the adverse event, important system issues necessary for long-term improvement continue unabated.

Many of the strategies employed to correct medication errors involve viewing individual process components. This usually takes the form of prescribing improvement, new dispensing systems, or improving patient compliance (Aparasu & Fliginger, 1997; Bergman & Wiholm, 1981; Dartnell et al., 1996; Nightingale et al., 2000). Component management operates in isolation from the medication use system as a whole and the intended impact may never be realized.

Adverse Drug Events

The term adverse drug event (ADE) has become popular due to a series of articles by researches from Harvard University (Bates et al., 1995b; Bates et al., 1997; Bates et al., 1995a; Bates et al., 1993; Cullen et al., 1995; Leape et al., 1991). The Harvard research team has defined an adverse drug event as "an injury resulting from the use of a drug" (Cullen, et al., 1995, p. 541). An ADE differs from an ADR in that it relaxes the "normal dosage" requirement and allows for causes other than the drug entity. The

definition does not, however, deal with the lack of drug use when medication therapy is clearly indicated.

The work done by the Harvard group has explored the idea of preventability. In one article, Leape et al. (1991) suggests that adverse effects are not random events but are system dependent. By looking at problems as system dependent, causes other than the drug product can be identified. Despite their discussion of systems issues, much of what the Harvard group terms preventable is attached to a finding of either negligence or error (Cullen et al., 1995). Negligence was defined as "care that fell below the standard expected of physicians in their community" (Brennan et al., 1991, p. 370). An error was defined as "a mistake in performance or thought" (Leape et al., 1991, p. 377). By looking for either negligence or error when assessing preventability, the tendency is to once again place blame and obscure system solutions.

The Harvard group employed intensive surveillance techniques using a research nurse to identify adverse drug events in hospitalized patients (Bates et al., 1995b; Bates et al., 1993; Leape et al., 1991). The evaluation of identified events and their preventability was accomplished through implicit physician review. While their results illuminate the problem of ADEs, this method would be nearly impossible to replicate in other settings. The difficulty in replication centers on two issues (Brennan, 2000). First, the results of an implicit evaluation may change based on the local standards of practice and expert opinion. Second, this method would be cost prohibitive for most organizations.

Drug-Related Morbidity

Drug-related morbidity (DRM) is a term I recommend for use to describe injury due to the misuse or lack of use of medications. Hepler and Strand (1990) have defined drug-related morbidity as the "clinical or biosocial manifestation of unresolved drug-

related problems" (p. 535). Thus, drug-related morbidity is preceded by a drug-related problem.

Drug-related problems are events or circumstances involving drug treatment that actually or potentially interfere with the patient achieving an optimal outcome of medical care (Hepler and Strand, 1990). Eight categories of drug-related problems have been identified by Strand et al. (1990). They include; 1) untreated indications, 2) improper drug selection, 3) subtherapeutic dose, 4) failure to receive drug, 5) overdose, 6) adverse drug reaction, 7) drug interactions, and 8) drug use without indication.

Drug-related problems signal a pattern of care that, if not changed, may lead to drug-related morbidity. These drug-related problems may serve as the impetus for monitoring plans to determine if medications are being used appropriately. Thus, efforts directed at understanding and correcting drug-related problems may slow or eliminate drug-related morbidity through changes in the medication use system at the earliest sign. If definitions exist that identify patterns of care indicative of a drug-related problem (serving as an indicator), prevention of drug-related morbidity is theoretically possible. By viewing drug-related problems as the precursor to drug-related morbidity, the connection of preventability to a finding of error is eliminated. This would allow practitioners to move beyond blaming simple causes, toward a quality assessment and improvement philosophy (Hepler & Grainger-Rousseau, 1995).

Hepler and Strand (1990) have proposed a method to evaluate preventability of drug-related morbidity. An adverse outcome attributable to drug therapy can be deemed preventable if

(1) the adverse outcome was preceded by a recognizable drug therapy problem,

(2) the adverse outcome of the drug therapy problem had been reasonably foreseeable,

(3) the cause of the adverse outcome could have been identifiable with reasonable probability, and

(4) the cause of the adverse outcome could have been reasonably controllable within the context and objectives of therapy.

Hepler and Strand's (1990) criteria for preventability offer a framework to develop explicit criteria that measure preventable drug-related morbidity. This would be offered in contrast to the labor-intensive and expensive use of experts currently relied upon in the literature.

Study Populations

Many of the studies published in the literature focus on events as they relate to hospitals or other institutional care. The focus on hospitals takes a limited view of the total amount of harm being done to patients (Brennan, 2000). The problems associated with outpatient care could be far more significant, although also more difficult to study and quantify (Weingart et al., 2000). There has not been a concerted effort to assess actual adverse drug reactions (and thus, drug-related morbidity) in ambulatory populations (Karch & Lasagna, 1975).

Research on adverse events in ambulatory patients is just beginning to garner attention. The volume of patients receiving care outside the hospital justifies the attention. Between 1983 and 1993, outpatient visits increased 75% while inpatient days declined 21% (Phillips et al., 1998). One study suggests that ambulatory patients have an adverse drug reaction rate of 2.5%, compared with an inpatient rate of 9% (Burnum, 1976). While the percentage for ambulatory patients may be lower, the actual number experiencing an adverse event is likely higher due to the volume of patient encounters.

It is also likely that ambulatory patients die from drug therapy at a rate not yet fully understood. Early data suggest that outpatient deaths would greatly increase current estimates (Leape, 2000). These factors support additional efforts directed at measuring preventable drug-related morbidity in ambulatory patients.

Measurement

Inconsistency of surveillance methodologies hinders the comparison of results across studies (Ross, 2001). Previously mentioned studies show large variations in their results. While some variation is due to different patient populations, much may be due to different surveillance techniques or definitions (Kramer et al., 1979; Ross 2001). There may also be differences in the scope of events monitored or the intensity of data collection (Caranasos et al., 1974; Hallas et al., 1990). There is a need for consistency in both the terminology and methodology of studies investigating preventable drug-related morbidity (Weingart et al., 2000; Ross 2001).

The screening mechanisms employed in the literature can be classified into one of three categories: implicit, structured implicit, and explicit (Ashton et al., 1999). Each is described and examples from the literature given.

Implicit

An implicit review in essence is peer review, with experts comparing the level of care provided to their own knowledge, opinions, and beliefs. The literature has many examples of studies where implicit judgement was used to determine the presence of drug-related morbidity (Bates et al., 1995b; Bates et al., 1993; Bero et al., 1991; Bigby et al., 1987; Hallas et al., 1992).

Adverse drug reaction studies have used implicit judgement for years. Kramer et al. (1979) state that

> the diagnosis of an ADR has usually depended on unspecific clinical judgement, arising from the subjective impression and previous experience of individual clinicians. (p. 623)

Thus, implicit review tends to be highly reviewer dependent and often has difficulty establishing significant conclusions due to the broad responses received from reviewers (Ashton et al., 1999; Karch et al., 1976; Thomas & Brennan, 2000).

There are also suggestions that implicit review is so subjective as to be invalid (Donabedian, 1978; Lipton & Bird, 1993). This may be especially true when an expert views the entire chart with the outcome known in advance (Caplan et al., 1991). Brennan (2000) states that physician judgements in the Harvard study may not be reliable. Other authors have also taken this position (Thomas & Brennan, 2000). One attempt to replicate the Harvard study resulted in drastically different results (Wilson et al., 1995). Additionally, implicit screening is very expensive and time consuming, limiting its usefulness for most health care organizations (Donabedian, 1978).

Structured Implicit

A second measurement technique is referred to as a structured implicit review. A structured implicit review combines the expert's internalized standards with directions that lead them to look at specific issues in care on which judgements are to be made (Ashton et al., 1999).

A common use for structured implicit review has been in the area of adverse drug reactions. Both the Naranjo et al. (1981) and Kramer et al. (1979) algorithms use a structured process to assist experts in judging the causality of adverse drug reactions. Each algorithm provides specific questions that direct practitioners to gather evidence in determining the probability of an ADR.

A structured implicit review may increase the reliability of the measure. This is due to the directing of experts to look for certain information in the patient's medical record. However, this method is still labor-intensive and costly.

Explicit

The final method of screening for drug-related events uses explicit criteria. Explicit criteria compare the actual care process against a set of statements or criteria that have been previously developed (Ashton et al., 1999). This method of surveillance is highly reliable and has good predictive validity (Ashton et al., 1999; Caplan et al., 1991). These are good characteristics for indicators of quality problems in the medication use system.

In addition to good measurement properties, practical support exists for the further development and testing of explicit criteria. Explicit criteria can be assembled into quality measures independent of the chart review process (Geraci et al., 1999). This allows the criteria to serve as an ongoing and consistent quality measure that does not rely on chart review and abstraction. Recent recommendations by the Institute of Medicine (1999) have listed the development of explicit criteria for measuring adverse medication events as a priority.

Despite the potential value of explicit criteria, there are some pitfalls. Explicit criteria are only as good as the development process. This can place criteria at one of two extremes; they can either be from leading experts using evidence-based literature, or they can reflect the average practice of local physicians (Donabedian, 1978). The burden of accuracy falls on the criteria and the biggest challenge is assuring that standards to which criteria are compared are valid (Ashton et al., 1999). Explicit criteria do not take into account individual patient care variability (Donabedian, 1978). This could be a

stumbling block for physician acceptance of explicit criteria to evaluate the quality of medication use if the organization uses them in a punitive manner.

Explicit criteria to evaluate prescribing in nursing home patients have been developed by Beers et al. (1991). These criteria were recently updated to include a broader classification of elderly patients (Beers, 1997). The work provides the opportunity to evaluate the prescribing of medications using explicit criteria developed by an expert panel. However, they only evaluated whether the drug was appropriate or not based on a global indicator. No attempt was made to incorporate clinical information or outcomes data.

Hanlon et al. (1992) attempted to develop explicit criteria as an index of appropriate medication use in the elderly. They used a ten-item scale that judged the decision making on a broader scale than Beers et al. (1991). However, there was no link to the patient outcome to determine the usefulness of the measure.

A recent study by MacKinnon (1999) developed definitions for preventable drug-related morbidity (PDRM) that linked the process and outcome. These definitions may be operationalized into explicit criteria and used to measure preventable drug-related morbidity with available information system technology. The strength of MacKinnon's (1999) work is the ability to detect both drug-related problems and adverse outcomes together. A measure of the outcome has been suggested as the only way to know is medication use is appropriate (Buetow et al., 1996).

Use of Computer Databases

The use of computers to store health care information has shifted from a financial focus to incorporate more clinical data. This shift offers additional research opportunities using administrative databases. One author has suggested more funding to research

secondary databases and less using primary data sources (Kralewski et al., 1994). In addition, the Institute of Medicine (1999) report has recommended the use of automation whenever possible. These factors support extensive growth in research using patient care databases.

Administrative data are being used to evaluate care (Paul et al., 1993; Romano & Mark, 1994). Administrative databases have advantages over primary data collection by allowing a more efficient review of a large number of cases, longitudinal data collection, long-term follow-up, a reduction in the cost of data collection, defined sampling frames, and the linkage of several databases (Jollis et al., 1993; Roos et al., 1991; Steinberg et al., 1990).

Administrative databases also have their drawbacks. The databases often do not include all the details involved in caring for patients, which may cause information to be lost (Roos et al., 1991). In addition, the accuracy of the database may suffer if information is either entered incorrectly or not entered at all (Romano & Luft, 1992). Despite these limitations, administrative databases have an important role in studying the outcomes of care (Romano & Luft, 1992).

The use of computers to screen patients for adverse events is receiving more attention as computer capabilities increase (Raschke et al., 1998). Computer screening of patient populations has been shown to detect more events than spontaneous reporting mechanisms currently in place (Bates et al., 1995; Evans et al., 1994). Automated screenings have also been shown to be more consistent than expert ratings (Camacho & Rubin, 1998). This could lead to consistency between organizations and allow benchmarking for future improvement initiatives. Thus, well-developed explicit criteria

used with an automated database may hold the key to system monitoring and ultimately for medication use improvements.

The use of computers to screen for preventable drug-related morbidity will also prove cost-effective. Rosenheck et al. (1999) estimated that in a Veterans Administration (VA) patient population it would cost between $150-300 per-patient-per-year to intensively monitor for adverse outcomes. This would add $174 million per year to the VA budget for screening alone. If, however, there were valid, explicit criteria that could be used with current computer technology, this cost would drop to $0.25 per-patient-per-year (Rosenheck et al., 1999). This cost difference would be significant, supporting the use of computers and explicit criteria in patient care research.

Early evidence suggests that computers can make a difference when monitoring patient events (Bates et al., 1995b; Bates et al., 1993; Christensen & Penna, 1995; Classen et al., 1991). These studies demonstrate that the use of computers with explicit definitions to measure preventable drug-related morbidity is possible. However, the next question will be assessing the validity and use of the measures.

Validity

Validity is an integrated evaluative judgement of the degree to which empirical evidence and theoretical rationales support the adequacy and appropriateness of inferences and actions based on measurement or other modes of assessment (Messick, 1989). In terms of drug-related morbidity as an indicator of the quality of medication use, validity is the degree to which the data indicating preventable drug-related morbidity identifies situations in which the quality of medication use is poor and can be improved (Nadzam, 1991). Rigorous assessment of validity in evaluating drug-related events has

not received much attention in the literature (Ross, 2001). Several issues related to validity are relevant to this discussion and are addressed in the pages that follow.

Triarchic Validity

The concept of validity has been evolving since the 1950s. Early in its development, validity was viewed as having separate components. These can be classified as content validity, criterion-related validity, and construct validity.

Content validity is based on professional judgements about the relevance of the content to a particular domain of interest, and about how completely and precisely the items or tasks represent that domain. Content validity is evaluated by showing how well the content samples the class of situations about which conclusions are to be drawn (Messick, 1989). Content validity does not measure actual performance, but rather is only a judgement based on expert opinion.

The second type of validity is criterion-related validity. Criterion-related validity is evaluated by comparing the measurement results with one or more external variables (called criterion) that provide a direct measure of the characteristic in question (Messick, 1989). The criterion is an existing "gold standard" by which the proposed measure is compared. Criterion-related validity is based on the degree of empirical relationship (correlation or regression) between the test scores and criterion scores. There are as many criterion-related validity measures as there are criterion.

Criterion-related validity can be divided into predictive and concurrent validity. Predictive validity indicates the extent to which future performance correlates with the current measure. Concurrent validity indicates the degree to which the measure estimates the present standing on the criterion.

The third validity category is construct validity. Construct validity is evaluated by investigating the qualities a test measures. Construct validity attempts to determine the degree to which certain explanatory concepts account for the measured results (Messick, 1989). Construct validity may use any evidence that affects the interpretation or meaning of the test scores. Almost any kind of information about a test may contribute to an understanding of construct validity, but is stronger if the degree of fit of the information with the theoretical rationale underlying score interpretation is explicitly evaluated.

Messick's Validity Framework

Validity has evolved into a unitary concept (Messick, 1989). This evolution does not allow validity to be neatly packaged into three different categories that serve as independent indicators of validity. The prevailing thought of having separate validity components has lead many (especially in health care) to use expert judgment of content as their sole assessment of validity, and thus to conclude that the instrument is valid for any use from that point forward.

Validity must involve a measure and an intended use. Without a measure, there is no assessment of validity (Messick, 1989). When validating a measure, what is being tested is not the observation device, but the inferences about the meaning of the score and the implications for actions taken based on that score.

Validity is also not complete after one, or even a few observations. Rather, validity is a matter of degree and builds over time as evidence gathers either for or against the particular use or observation. Thus, validation is essentially a matter of making the most reasonable case to guide both the current use of a measure and research to advance understanding of what the score means.

According to Messick (1989),

> what is needed is a way of cutting and combining validity evidence that forestalls undue reliance on selected forms of evidence, that highlights the important though subsidiary role of specific content- and criterion-related evidence in support of construct validity in testing applications, and that formally brings consideration of value implications and social consequences into the validity framework. (p. 20)

Messick (1989) attempts to meet this challenge by proposing a unified validity framework distinguishing two interconnected facets. One facet is the source of justification of the measure (primarily based on appraisal of either evidence or consequence). The second facet is the function or outcome of the measure, being either interpretation or use. Messick (1989) proposed a two-by-two table in which each block is linked to the information used to satisfy it (see Figure 2.3).

The evidential basis for interpretation of a measure requires what we commonly refer to as construct validity. The evidential basis of the use of a measure also looks to construct validity, but is supported by evidence for the relevance of the measure to the specific purpose (i.e., content validity) and for the utility of the measure in the applied setting. Because content and criterion-related validity contribute to score meaning, they have come to be recognized as aspects of construct validity (Messick, 1989).

	Interpretation	Use
Evidential Basis	Construct validity	Construct validity + relevance/utility
Consequential Basis	Value implications	Social consequences

Figure 2.3: Messick's Facets of Validity (Messick, 1989, p.20)

The consequential basis for interpretation of a measure is an appraisal of the value implications of the construct label, of the theory underlying the interpretation, and the ideologies in which the theory is imbedded. A central issue is whether or not the theoretical implications and the value implications of the interpretation of a measure are commensurate, realizing that value implications are tied to score meaning.

The consequential basis for the use of the measure is the appraisal of both potential and actual social consequences. The social consequences are important to anything we are validating that may have an impact on society or policy. Value and social consequences are rarely considered when assessing validity.

Preventable Drug-Related Morbidity and Validity

When assessing the validity of a measure of preventable drug-related morbidity, evidence can be gained through theoretical links that have been established in the literature. Risk factors for patients who experience preventable drug-related morbidity have been studied. Risk factors are variables that are statistically related to the adverse event. Risk factors that are related to the presence of PDRM should be more prevalent in patients with an instance of preventable drug-related morbidity than in those patients without an instance. The following items represent risk factors identified in the literature and shown to be significant in MacKinnon's (1999) study.

Number of Medications

The number of medications a patient receives has been studied on several occasions. Studies suggest that the more drugs a patient is taking, the more likely they are to experience an adverse event (Classen et al., 1991; Colley & Lucas, 1993; Gandhi et al., 2000; Hallas et al., 1992; Hanlon et al., 1997; Hurwitz, 1969; Lakshmanan et al., 1986; MacKinnon, 1999; Smith et al., 1966).

Number of Prescribers

The number of prescribers has been show to be a risk factor by Colley and Lucas (1993) and MacKinnon (1999). A patient with more prescribers has a higher risk for PDRM. This may be due to poor communication between prescribers and a lack of information on the part of each prescriber.

Cardiovascular Drugs

Studies by Hanlon et al. (1997), Lindley, et al. (1992) and Bates et al. (1999) identify cardiovascular drugs as a risk factor for adverse events. Escobedo and Zach (1996) and MacKinnon (1999) specify the category of antihypertensive drugs as significantly associated with adverse events.

Gender

The issue of gender is less clear. Studies by Hallas et al. (1992), Lakshmanan et al. (1986) and Hurwitz (1969) state that females are more likely to experience an adverse event. This is in direct contrast to the MacKinnon (1999) study, which identified males as being more likely to experience preventable drug-related morbidity.

Number of Diagnoses

The number of diagnoses has also been identified as a risk factor. Studies indicate that a patient with more co-morbidities has a higher likelihood of experiencing an adverse event (Gandhi et al., 2000; MacKinnon, 1999; Smith et al., 1966; Trunet et al., 1980).

Age

Age has been identified in previous studies as a risk factor for adverse drug events (Brennan et al., 1991; Classen et al., 1991; Colley & Lucas, 1993; Hallas et al., 1992; Hanlon et al., 1997; Hurwitz, 1969; Lakshmanan et al., 1986; Thomas & Brennan, 2000;

Weingart et al., 2000). When studying an elderly population, chronological age may not be as important. However, patients over 85 (oldest of the old) may be of interest. It has been shown that patients over 85 are at a higher risk of PDRM than those between 65-85 (Gurwitz & Avorn, 1991).

Health Care Resource Utilization and Cost

Studies indicate that drug-related morbidity increases the utilization of health care resources and the cost of caring for patients (Bates et al., 1993; Dartnell et al., 1996; Hanlon et al., 1997; Karch & Lasagna, 1975; Lakshmanan et al., 1986; Ornstein et al., 1999; Tafreshi et al., 1999; Thomas et al., 1999). Thus, patients with preventable drug-related morbidity should access the health care system more (in terms of hospitalizations, emergency room visits, physician office visits and medication use) than patients without PDRM. In addition, patients with PDRM should have higher direct medical costs than those without. This cost could be incurred by the health care system (thus, the payer) or from the patient in the form of co-pays and deductibles.

CHAPTER 3
METHODOLOGY

Introduction

The study was divided into four phases to accomplish the objectives listed in Chapter 1. The first phase of the study involved defining specific scenarios of preventable drug-related morbidity (PDRM). The second phase operationalized the specific definitions of PDRM for application to a computer database. Phase III measured preventable drug-related morbidity in an elderly population and gathered evidence for validity of the definitions. The final phase used the measure of PDRM in a root cause analysis to determine their usefulness in quality assessment and improvement.

All four phases of our study were accomplished with the aid of a large managed care organization (MCO). The managed care organization was selected because of their elderly patient population (a Medicare product), available database, and patient information across the continuum of care. Additionally, the managed care organization was interested in new methods of evaluating drug use to improve care, enhance their position in the market, and bolster their accreditation survey preparation.

Phase I: Defining Preventable Drug-Related Morbidity

Delphi Panel

Phase I of the study employed a Geriatric Medicine Expert Panel to define explicit scenarios of preventable drug-related morbidity. The expert panel used the Delphi technique to come to consensus on proposed definitions of PDRM. The Delphi

technique was developed in the 1948 by the Rand Corporation as a means to obtain expert opinion in a systematic manner (Fink et al., 1984).

The Delphi technique eliminates interpersonal interactions as the controlling variable in group decision making (Goodman, 1987). The intent is to foster discussion and judgement on preventable drug-related morbidity so the decisions made represent the panel's views. By using the Delphi technique with a panel of physicians, the drawbacks of traditional committee structures are counteracted, including a domineering personality, the unwillingness to be seen as disagreeing, and the vocal minority (Goodman, 1987).

The selection of panel members is critical if the Delphi panel is to function properly (Duffield, 1993; Fink et al., 1984). A total of seven (7) physicians were chosen for the panel (see Appendix A). The managed care organization's regional medical director and principal investigator (RJF) selected panel members. Physicians were chosen based on their expertise in geriatrics, practice with the managed care organization's Medicare patients, and their willingness to participate.

During the survey process, it became necessary to disqualify one panel member (see Chapter 4). The disqualification was based on the physician's lack of support for the project. This determination was made after reviewing the physician's response to the surveys and a face-to-face meeting with the principal investigator (RJF). Another physician was selected as a replacement.

MacKinnon's Definitions

The specific scenarios for preventable drug-related morbidity built upon previous work done by MacKinnon (1999). MacKinnon (1999) used literature review and an expert panel to create 52 operational definitions of preventable drug-related morbidity. All definitions have two components: a pattern (i.e., process) of care and an associated

adverse outcome. MacKinnon's (1999) fifty-two definitions served as the content for the first survey. In addition to the 52 definitions, three scenarios rejected by MacKinnon's (1999) panel were included in the original Delphi survey. The original content for all definitions from MacKinnon's (1999) panel remained unchanged for the first survey.

Panel members were asked to vote (yes or no) whether they believed a certain scenario represented an instance of preventable drug-related morbidity (see Appendix B for complete instructions given to panel members). The results of each survey were compiled and comments made in support of their decision were recorded. The voting results and comments were used to in subsequent rounds. Scenarios receiving the majority of panel member's support were included in the next survey. The process continued until consensus did not change appreciably.

Phase II: Operationalizing Definitions

Phase II of the study focused on operationalizing the consensus-approved definitions for measurement in an administrative database.

The managed care organization (MCO) uses computer technology to gather patient encounter information from physician offices, hospitals, pharmacies, and other care sites in their network. Information is communicated between the care site and the MCO using a standardized coding system. The coding of health care encounters is accomplished through a set of standards called the International Classification of Diseases-9th edition (ICD-9) and Current Procedural Terminology (CPT) codes (Banks et al., 1999; Harris & Gordy, 1998). ICD-9 coding uses the diagnosis as its base for recording encounters. So-called diagnostic coding is the primary means in today's health care environment for submission of patient care claims. ICD-9 codes are available from

hospitals, emergency rooms, physician offices, long-term care facilities, and skilled nursing facilities.

Current Procedural Terminology (CPT) codes are based on ambulatory services rendered to a patient, often in a physician's office. CPT coding is a systematic listing of procedures and services performed by physicians (Harris & Gordy, 1998). CPT codes are specific to the actual services a patient receives at an ambulatory care site. These codes are also communicated between the care sites and the MCO.

Medical Event Coding

The current system used to code health care encounters is very complex (Christensen & Penna, 1995). This coding system was designed years ago with financial reimbursement as the primary function (Diehr et al., 1999). The focus on financial aspects has hindered the utility of codes for other activities, such as clinical evaluation or research. When using coded data for reasons other than financial, outside expertise is needed to understand and overcome inherent difficulties. The recommended procedure is to use experienced medical record coders and a physician or other clinical expert (Steinberg et al., 1990).

Operationalizing the definitions properly is crucial for application to the managed care organization's database. It is important that the codes selected for each definition be accurate and complete. Two medical record coders were chosen to operationalize the definitions for the study. The medical record coding personnel (coders) were chosen based on their training, expertise, and willingness to participate. A medical record administrator employed by a university hospital assisted in the selection of the participants.

Each coder was given the 49 definitions agreed upon by the Geriatric Medicine Expert panel. The coders worked independently to select all appropriate codes (ICD-9 and CPT). The coders were instructed to assign the ICD-9 code with the least number of digits possible to properly identify the pattern or outcome of care. This is done to reduce coding biases (Romano & Luft, 1992; Steinberg et al., 1990).

The principal investigator (RJF) compiled a list of all codes chosen by at least one coder. For each definition, the percent agreement between the coders was calculated. The percent agreement equals the number of codes identified by both coders divided by the total number of codes. An overall mean and standard deviation for the coding process was calculated based on the percent agreement for each definition.

All codes selected by the coders were sent to a physician for review. The physician was instructed to review each definition and all codes. He assigned a value to each code based on its consistency with the definition. The following three-point scale was used; 1) the code is definitely consistent with the definition, 2) the code is possibly consistent with the definition, or 3) the code is not consistent with the definition. Codes receiving a 1 or 2 were collapsed into a category "consistent with the definition." Codes that received a score of 3 were eliminated. The final ICD-9 and CPT codes remaining were used to measure PDRM in the patient population.

Medication Coding

Medications were coded for each definition using National Drug Codes (NDC). Lexicon® from Multum (www.multum.com) was used to obtain all NDC numbers for the targeted medications. Multum provided a mechanism to identify all appropriate NDC numbers based on the individual medication or class of medications.

One of the risk factors in the study was "patients receiving a cardiovascular medication." Because of the broad nature of this category and the number of NDC numbers that would be required, a method other than NDC codes was used. The managed care organization's database attaches an American Hospital Formulary Service (AHFS) number to each medication. The AHFS classification number is a systematic coding mechanism for classes of medications. One such class is cardiovascular drugs, which allowed easy identification of the targeted medications. AHFS numbers were only used for this risk factor.

Phase III: Measurement of Preventable Drug-Related Morbidity and Validity

Phase III of the study measured the prevalence of preventable drug-related morbidity in an ambulatory Medicare population. Additionally, evidence to validate the definitions was gathered.

Study Period and Population

The data collection period totaled 18 months, from April 1, 1998 to September 30, 1999. The study population consisted of all patients over the age of 65 who were enrolled in the managed care organization's Medicare product for at least 12 months of the study period. The elderly were chosen for study due to their higher drug use and the higher likelihood of drug-related problems (Caranasos et al., 1974; Culler et al., 1998; Hurwitz, 1969).

The elderly may be particularly well suited to using administrative data. Claims records capture clinical conditions more often in patients over 64 than in those 64 years of age or less (Jollis et al., 1993). This is primarily due to the presence of chronic conditions. Data quality has also been shown to improve as more data points are collected over a longer period of time (Roos et al., 1991).

Managed Care Database

The managed care organization gathers data across the entire continuum of care (hospitalizations, physician office visits, emergency room encounters, drugs, etc.). Gathering information across the continuum of care strengthens the study. Many elderly patients have chronic conditions that may not require hospitalization for a long period of time. Thus, matching the inpatient and outpatient care records allows a complete view of patient care (Romano & Luft, 1992).

Partnering with a private managed care organization with a Medicare product offers additional advantages. The managed care organization's database captured all ICD-9 codes for each patient. When exchanging information directly with Medicare, ICD-9 codes are limited to 5 diagnoses (Steinberg et al., 1990). This can lead to lost information when using a database for research purposes. It has been shown that 9 or more ICD-9 codes reduce the problem of under-representation brought about by this truncation (Romano & Mark, 1994). The managed care database did not limit the number of diagnoses or procedures codes collected.

Data Fields

The data were received from the managed care organization as two separate databases, one for medical claims and the second containing pharmacy claims. Each database contained the identical blinded patient identifier that could not be traced back to the individual patient.

The following data fields were captured from the medical claims database.

- *Unique patient identification:* Data were stored in a patient specific manner. For purposes of the study, any means by which an individual patient could be identified was eliminated. The managed care organization has a unique identification code for each patient. This code was used to create a new identification number to eliminate issues with confidentiality. The algorithm for

coding was kept at the managed care organization and was not available to the primary researcher (RJF).

- *Coverage period*: Each patient had enrollment dates for insurance coverage. Patients enrolled for at least 12 months during the study period were included.

- *Gender*: Patient gender was available in the database as male and female.

- *Patient age*: Each patient's birth date and chronological age was captured.

- *Health care encounters*: Patient health care encounters were coded based the care site, diagnosis, and the services/products rendered to the patient. These were in the form of ICD-9 and CPT codes.

- *Health care costs*: The managed care organization database recorded the amount paid for each specific health care encounter or procedure performed from the payer's perspective. A separate field records any co-pays or deductibles paid by the patient.

- *Date of service*: The database recorded the date (beginning and end) of each encounter.

The following data fields were captured from the pharmacy claims database.

- *Unique patient identification:* As mentioned, data are stored in a patient specific manner. A unique identification code for each patient was provided, which matched that in the medical claims database. This field was used to merge the databases.

- *Drug identification*: National Drug Code (NDC) numbers were used to identify drug use for all definitions. An additional field records the American Hospital Formulary Service (AHFS) classification for each medication. The AHFS code was useful for identifying cardiovascular drug use.

- *Prescriber identification*: Each prescriber was assigned a unique code which was recorded for each new prescription.

- *Fill date*: Each prescription had the date filled in the database. There was a date for both new prescriptions and each refill date.

- *Cost*: The cost of the medication was recorded for each prescription. The cost was separated into direct expense to the managed care organization and any patient co-pays or deductibles.

Study Variables

Preventable drug-related morbidity

The primary variable of interest was the presence of preventable drug-related morbidity. The measurement of preventable drug-related morbidity involved the identification of a pattern of care and the corresponding outcome. The pattern of care and outcome were identified independently. Patients with both the pattern of care and the outcome for each consensus-approved definition were counted as a PRDM event.

Risk factors

As discussed in chapter 2, several factors are related to the presence of PDRM. These were used as confirmatory risk factors in the study. Each risk factor was operationalized as follows:

- The number of different medications taken during the 4 months preceding the PDRM event were counted and operationalized as a dichotomous variable. Patients receiving 6 or more medications received a 1, zero (0) otherwise.
- A patient with 4 or more unique prescribers was classified as a 1, while a patient with 3 or less was assigned a value of zero (0).
- Patients receiving cardiovascular drugs were classified as a 1, zero (0) otherwise.
- For purposes of this study, females were assigned a value of 1, males zero (0).
- The number of diagnoses was operationalized a dichotomous variable. A patient with 4 or more diagnoses was classified as a 1, zero (0) otherwise.
- Age was classified as dichotomous variables with patients over 85 (oldest of the old) classified as a 1, zero (0) otherwise.

Health care resource use and costs

Health care resources and costs were operationalized as follows:

- The number of hospitalizations is equal to the number of individual hospitalizations during the study period. The cost of hospitalization was

recorded as those incurred by the managed care organization (MCO) and any patient co-pays or deductibles.

- The number of emergency room (ER) visits was equal to the number of times the patient visited the ER during the study period. Once again, cost was recorded as that paid by the MCO and any patient co-pays or deductibles.

- The number of physician office visits was recorded during the study period. The cost was that incurred by the MCO and any co-pays or deductibles covered by the patient.

- Medications were recorded as the number of unique prescription drugs a patient received during the 4 months preceding their PDRM event (if applicable). Patients without an instance of PDRM had the number of medications recorded during the first four months of enrollment. The total cost is that incurred by MCO and any co-pays or deductibles covered by the patient over the study period.

- The total cost of care is the sum of the direct medical expenses covered by the MCO and the patient.

Phase IV: Root Cause Analysis

An expert panel was convened to determine if the measure of preventable drug-related morbidity could be used in a quality assessment and improvement framework. A root cause analysis was conducted to determine if practitioners could reason the underlying causes of quality problems for the ten most common instances of PDRM.

The expert panel conducting the root cause analysis consisted of 4 physicians and 2 pharmacists (Appendix C). The ten most commonly detected PDRM events in the patient population were presented to the panel. The panel was also given introductory information about the study objectives and the process of root cause analysis. The panel was asked to develop cause-and-effect diagrams for any of the ten most common consensus-approved definitions of preventable drug-related morbidity.

A quality improvement consultant from the managed care organization facilitated the root cause analysis. An outside consultant was employed to observe group

interactions that took place during the root cause analysis. In particular, the consultant was asked to observe the consensus building during the meeting.

Statistical Analysis

Preventable Drug-Related Morbidity

Preventable drug-related morbidity was the primary measure of interest. The rate of preventable drug-related morbidity in our population was equal to the number of patients with at least one instance of preventable drug-related morbidity, divided by the total number of patients eligible for the study. Because the study viewed up to 18 months of data, the number of patient years represented by the population was calculated. The prevalence of preventable drug-related morbidity was equal to the number of patients with PDRM events detected divided by the number of patient years.

Factors Associated With Validity

Variables related to PDRM from previous studies served as evidence of validity of the definitions. Eleven variables were studied as confirmatory hypotheses. The variables were broken down into risk factors and health care resource use.

Risk factors as confirmatory hypotheses

The following are confirmatory hypotheses for the risk factors:

1. Females will tend to experience preventable drug-related morbidity more than males.
2. Patients receiving 6 or more medications will experience preventable drug-related morbidity more often than those receiving less than 6 medications.
3. Patients receiving cardiovascular medications will have a higher rate of preventable drug-related morbidity than those who are not.
4. Patients with 4 or more prescribers will experience preventable drug-related morbidity more than those with less than 4 prescribers.

5. Patients with 4 or more diagnoses will experience preventable drug-related morbidity more often than those with less than 4 diagnoses.

6. Patients 85 and older will experience preventable drug-related morbidity more often than those under 85.

The presence of risk factors was assessed using a logistic regression model. Logistic regression has been used in previous studies to examine adverse drug events and risk factors (Bates et al., 1999; Escobedo & Zack, 1996; MacKinnon, 1999; Seeger et al., 1998). Both bivariate and multivariate models were used in the study.

In the bivariate analysis, each risk factor was examined as an independent variable with the presence of PDRM as the dependent variable. A multiple logistic regression model was used where all risk factors shown to be significant in the bivariate analysis were entered simultaneously to determine multivariate significance.

Significance in logistic regression models was determined by those variables with an odds ratio of greater than one or less than one at the $p = .05$ level. Positive associations with the presence of preventable drug-related morbidity are those variables with an odds ratio greater than one. Those variables with an odds ratio less than one were considered negatively associated with preventable drug-related morbidity.

Resource use as confirmatory hypotheses

As described previously, patients who experience preventable drug-related morbidity are also likely to use more health care resources. The following are confirmatory hypotheses for resource use:

7. Patients with preventable drug-related morbidity will tend to have more emergency department visits than those without.

8. Patients with preventable drug-related morbidity will tend to have more hospital admissions than those without.

9. Patients with preventable drug-related morbidity will tend to have more doctor office visits than those without.

10. Patients with preventable drug-related morbidity will tend to cost more in total direct health care dollars than those without.

11. Patients with preventable drug-related morbidity will tend to have higher medication costs than those without.

To test these confirmatory hypotheses, a bivariate logistic regression model was used. All tests for significance are at the $p = .05$ level.

Pattern of Care and Outcome Analysis

The measurement of preventable drug-related morbidity involved identification of a pattern of care and outcome. Linking the pattern of care with the outcome in patients adds to the validity of the explicit definitions. By identifying the pattern of care independent of the outcome, additional analysis was possible for each definition. For each definition, patients could be classified into one of four categories:

- The patient had both the pattern of care and the corresponding outcome, and thus preventable drug-related morbidity;
- The patient had only the pattern of care present without the corresponding outcome;
- The patient had only the outcome detected; or
- The patient had neither the pattern of care or outcome detected.

Patients with evidence of PDRM and those with the only pattern of care were of most interest for the studies purpose. Those patients with only the outcome present will be discussed briefly.

Days Between the Pattern of Care and Outcome

The pattern of care and corresponding outcome identified had the date of occurrence recorded. The number of days between the pattern of care and corresponding

outcome was calculated. This measure is referred to as the Number of Days from Pattern of care to Outcome (NDPO). Each consensus-approved definition with more than one instance of preventable drug-related morbidity detected in the population had a mean and standard deviation for NDPO calculated.

Patients with only the pattern of care detected but not the adverse outcome also had the date of occurrence attached. A calculation was made to determine the number of days between the pattern of care and the end of the study (September 30, 1999). This measure was useful because the pattern of care may not have had adequate time to culminate in the adverse outcome. To adjust for this bias, a cut-off point was sought to estimate the number of days, for each definition with 10 or more PDRM instances, where the pattern of care would be expected to result in an adverse outcome. A cut-off point was determined to be the number of days where 95% of the patterns of care would be expected to result in the corresponding outcome.

The observed distribution of the NDPO for each definition with 10 or more instances was examined using the normal distribution, the exponential distribution and the gamma distribution. None of the observed distributions appeared to fit the normal distribution. The gamma distribution did not prove useful. The two methods chosen were linear interpolation of observed data and the cumulative exponential distribution. Linear interpolation estimated where the 95% score occurred in the population. The exponential distribution used the cumulative function to determine the 95% cut-off point. Patients with the pattern of care only where the number of days to the end of the study was longer than the cut-off point were included in additional calculations of the association between the pattern of care and the outcome.

Process-To-Outcome Value

A Process-To-Outcome Value (PTOV) for each definition with at least ten instances was calculated. The PTOV represents the proportion of patients with the pattern of care (after adjustment) that also had the corresponding outcome. A high PTOV value signifies a strong association between the pattern of care and the corresponding outcome. The pattern of care criteria may be valid if it can be demonstrated that what is classified as poor process by the assessment method is associated with poor outcomes (Ashton et al., 1999).

CHAPTER 4
RESULTS

Overview

The results of the study will be presented in four sections. The Geriatric Medicine Expert Panel and the consensus-approved definitions of preventable drug-related morbidity (PDRM) will be presented first. The second section will give the results of the operationalization of the definitions. Thirdly, the measurement of PDRM and associated variables in the study population will be detailed. Finally, the root cause analysis will be presented as a demonstration of the use of a PDRM measure in quality assessment and improvement.

Geriatric Medicine Expert Panel

The Delphi technique was used to develop consensus within the Geriatric Medicine Expert Panel on definitions of preventable drug-related morbidity (PDRM). The initial survey listed 55 explicit definitions of preventable drug-related morbidity: 52 definitions adopted from MacKinnon's (1999) study and three (3) definitions that had been rejected by MacKinnon's (1999) expert panel. Consensus of the panel was obtained after three rounds. Appendix D contains the final list of 49 consensus-approved definitions of preventable drug-related morbidity: 44 adopted from MacKinnon's (1999) study, 2 that had been rejected by MacKinnon's (1999) panel, and 3 new scenarios suggested by individual panel members and accepted by the group.

Mnemonics

A series of mnemonics have been created to facilitate the presentation and discussion of the results. Appendix E lists the full mnemonic for each definition. In Appendix E the mnemonics are listed with the outcome first, followed by a forward slash, then the pattern of care. If there is more then one component in the pattern of care, each is separated by a dash (outcome/pattern1-pattern2). Appendix F contains an alphabetical list of the mnemonic components. The definition number and the mnemonic will be used most often when presenting and discussing the results.

MacKinnon's Definitions Accepted by the Panel

The panel accepted 44 of the 52 definitions taken from MacKinnon's (1999) study. Table 4.1 lists the eight definitions rejected. Two of the definitions rejected by the panel relied on measuring glycosylated hemoglobin (HbA_{1c}) levels to prevent acute glycemic events (either hyperglycemia or hypoglycemia). In both cases, the panel felt that HbA_{1c} levels were not good predictors of acute events. Panel members cited literature and argued that poor blood glucose control may not be reflected in a patient's glycosylated hemoglobin (HbA_{1c}) level in time to prevent an acute attack. In fact, it takes 1-6 weeks for poor blood glucose control to be reflected in the patient's HbA_{1c} level (DiPiro et al., 1999; Gebhart et al., 1991). Thus, HbA_{1c} levels are more reflective of chronic blood glucose control and not a good predictor of acute events. Blood glucose monitoring is still recommended for the detection and avoidance of acute events (DiPiro et al., 1999). Panel members recommended that fingersticks would be an acceptable pattern of care for the scenario. However, daily blood glucose monitoring could not be measured in the existing administrative database. Thus, the recommended scenario was not included.

Two other definitions rejected by the panel had a fall with a broken bone as the outcome linked with a pattern of care that involved the use of either antipsychotic or anticholinergic drugs. In both cases, the panel did not feel the association between the drug use and the adverse outcome was strong enough to accept the proposed definitions.

The use of beta-blockers in patients with a history of congestive heart failure was also rejected as an instance of PDRM by the panel. Between the time MacKinnon's (1999) panel developed these definitions and the current panel's work, evidence emerged to accept, and even promote, this pattern of care (Cohn, 2000; DiPiro et al., 1999; Tsuyuki et al., 2000). The panel cited this new evidence in support of their rejection of the scenario.

The panel had similar reasons for rejecting the other definitions. The panel rejected these events due to the lack of a strong direct correlation between the adverse outcome and the pattern of care, or the need to have a pattern of drug use for a patient population (such as beta-blockers in diabetic patients).

MacKinnon's Rejected Definitions

As a check between panels, three definitions rejected by MacKinnon (1999) were inserted into the first survey. By the end of the third survey, two of the three definitions remained. The one definition rejected by both panels was:

Outcome: Fall and/or hip fracture and/or bone break

Pattern of care: Use of a nitrate (e.g., isosorbide, etc.)

Panel members rejected this scenario based on the weak correlation between the use of nitrates and a patient fall, with or without a broken bone. There are several variables that could be responsible for a patient fall (Gales & Menard, 1995).

Table 4.1: Original Scenarios Rejected by the Panel

Clinical scenario	
Outcome:	ER visit/hospitalization due to hyperglycemia
Pattern of Care:	1. Use of an oral hypoglycemic agent (e.g., chlorpropamide, etc.) 2. Hemoglobin A1c level not done at least every 6 months
Outcome:	ER visit/hospitalization due to hypoglycemia or hyperglycemia
Pattern of Care:	1. Use of insulin 2. Hemoglobin A1c level not done at least every 6 months
Outcome:	Fall and/or hip fracture and/or bone break
Pattern of Care:	Use of an antipsychotic (e.g., thioridazine, haloperidol, chlorpromazine, etc.)
Outcome:	Fall and/or hip fracture and/or other bone fracture and/or bone break
Pattern of Care:	Use of an anticholinergic agent
Outcome:	ER visit/hospitalization due to systolic heart failure
Pattern of Care:	1. History/diagnosis of systolic heart failure 2. Use of beta-adrenergic blocking agent (e.g., propranolol, nadolol, etc.)
Outcome:	ER visit/hospitalization due to extreme hypoglycemia
Pattern of Care:	1. History/diagnosis of diabetes 2. Use of beta-adrenergic blocking agent (e.g., propranolol, nadolol, etc.)
Outcome:	ER visit/hospitalization due to congestive heart failure
Pattern of Care:	1. History/diagnosis of congestive heart failure 2. Use of a calcium channel blocker (e.g., diltiazem, etc.)
Outcome:	Gastritis and/or upper GI bleed and/or GI perforation and/or GI ulcer and anemia
Pattern of Care:	1. NSAID use for at least 1 month 2. No concurrent use of a cytoprotective agent (misoprostol) 3. Hemoglobin/hematocrit/CBC not done within 30 days of the start of therapy or not done at least every three months thereafter.

NOTE: Scenarios were taken from MacKinnon's (1999) study

The two definitions rejected by MacKinnon's (1999) panel that were accepted by the current panel included definition 31 (Dig/Dig-BUNCr-Druglvl) and 40 (ARnF/Allp-BUNCr). Both definitions have support in the literature as an instance of PDRM (Abad-Santos et al., 2000; Kumar et al., 1996).

Delphi Panel Survey Results

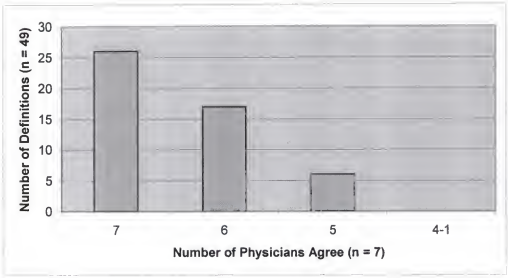
Three rounds of surveys were needed to attain consensus within the Delphi panel. The panel's level of agreement improved with each survey (see Table 4.2). The percentage of all definitions having 83% or more of the panel voting in agreement (i.e., voting that a scenario was an instance of PDRM) increased from 63.6% in round 1 to 87.8% in round 3. The percentage of definitions with 50-71% affirmative votes and those with less than 50% (which were rejected) declined with each survey.

Table 4.2: PDRM Definitions Receiving Percent of Agreement Votes

Panel members agreeing	Round 1	Round 2[b,c]	Round 3
83% or more	63.6% (35)[a]	69.8% (37)	87.8% (43)
50-71%	27.3% (15)	22.6% (12)	12.2% (6)
Less than 50%	9.1% (5)	7.6% (4)	0.0% (0)

[a]Percent of proposed definitions receiving the level of agreement from panel members
[b]One panel member changed between rounds 1 and 2
[c]There were 6 panel members included in round 1, and 7 for rounds 2 and 3.
NOTE: PDRM: preventable drug-related morbidity

Figure 4.1 illustrates the level of agreement after the third round by showing the number of physicians that felt a scenario was an instance of preventable drug-related morbidity. Out of the 49 definitions, 26 had all seven panel members agreeing it was an instance of PDRM, 17 had six out of seven, and 6 had five out of seven. No definition received less than five members agreeing it was an instance of preventable drug-related morbidity. This level of agreement was judged sufficient to end the Delphi process after the third survey and accept 49 scenarios as explicit definitions of PDRM.



NOTE: No definition received less than 5 votes in round 3

Figure 4.1: Number of Physicians Agreeing a Scenario is an Instance of PDRM

Individual Panel Member Voting Results

The voting pattern for each panel member demonstrated change during the Delphi process. Table 4.3 lists each individual physician's percent of scenarios he felt was an instance of PDRM in each round.

In round one of the Delphi process, the percent of scenarios accepted by each physician ranged from 54.5%-90.9%, with an average of 76.4%. Round 2 showed an improvement, with a range of 71.7%-100%, and an average of 87.8%. The final round demonstrated slight improvement with a range and average of 81.6%-100% and 92.7%, respectively.

The percent of definitions each panel member agreed was an instance of preventable drug-related morbidity increased with each survey. The range of percentage point increase per physician was 4.5-27.1, with an average increase of 15.2. Thus, all panel members progressed in their level of agreement with each round.

Table 4.3: Individual Panel Member Percent Agreement

Panel member	Round 1	Round 2	Round 3
1	87.3% (48)	92.4% (49)	91.8% (45)
2	87.3% (48)	98.1% (52)	100.0% (49)
3	90.9% (50)	100.0% (53)	100.0% (49)
4	N/A[a]	83.0% (44)	93.8% (46)
5	72.7% (40)	86.7% (46)	93.8% (46)
6	54.5% (30)	71.7% (38)	81.6% (40)
7	65.5% (36)	83.0% (44)	87.7% (43)

[a]Panel member number 4 was changed between rounds 1 and 2

Disqualification of Panel Member

After round 1, the surveys and comments were reviewed and tabulated. Based on written comments, it was evident that one panel member did not agree with the goals of the study. Because of this member's interpretation of the study, all panel members received retraining on the goals and process of the study.

The retraining of the panel took place in one-on-one meetings with the principal investigator (RJF). The meetings followed a structured agenda that reviewed the goals of the study, the definitions and framework of the survey, the instructions for completing the survey, and open time for questions.

Based on the first survey, the individual meeting, and the response on the second survey, it became necessary to disqualify the previously mentioned panel member. During the one-on-one meeting, it was clear that this particular panel member would not support the goal of the project. During that meeting he stated, "I don't care what you say these definitions will be used for, I know that *[MCO name]* will use them as practice standards and tell me I am not doing things right."

After the disqualification of the panel member, a replacement was selected. This panel member received the same instructions as other panel members (both written and

oral). Sitting panel members were not informed of the disqualification or the new panel member. The new panel member began by completing the second survey.

Operationalization of Definitions

The consensus-approved definitions of preventable drug-related morbidity were operationalized for application to an administrative database. The pattern of care and outcome for each definition were coded separately. Diagnosis and medical-related procedures were coded using International Classification of Diseases-9th edition (ICD-9) and Current Procedural Terminology (CPT) codes. National Drug Codes (NDC) were used to identify medication use.

Medical Event Coding

Two medical record coders independently selected all possible ICD-9 and CPT codes for each pattern of care and corresponding adverse outcome. The two sets of codes were combined and any code selected by at least one coder was included as a possible code for each definition.

The medical record coders identified the same codes approximately 60% of the time (standard deviation of 27.1). The range of identical codes selected by both coders varied from 0-100%. The extreme values were more likely to occur when the coders identified fewer total codes per definition.

Overall, the medical record coders identified a total of 6,536 unique codes for the 49 definitions. The number of codes identified for each definition ranged from 1 to 843. The average number of codes identified per definition was 133.4 with a median value of 31, reflecting a skewed distribution to the right.

Physician Review of Codes

The codes identified by the medical record coders were given to a physician for clinical judgment as to whether each code was consistent with the consensus-approved definition. The physician reviewer judged 4,497 of the 6,536 codes (68.8%) as definitely consistent with the definition, 747 (11.4%) codes as possibly consistent with the definition, and 1,292 (19.8%) of the codes as not consistent with the definition. All codes deemed not consistent with the definition were eliminated. The percent of codes eliminated per definition ranged from 0-53.9%.

Preventable Drug-Related Morbidity Measurement

Study Population

Overall, there were 11,711 patients eligible for inclusion in the study. The majority of the study population were female (57.3%). The average age of participants was 73.8 years, with approximately 11% of the study population 85 years or older.

Patients were covered by the managed care organization an average of 1.32 years during the 18-month study. Thus, the 11,711 patients accounted for 15,458.5 patient years.

Preventable Drug-Related Morbidity

Of the 11,711 patients, 966 (8.2%) had at least one instance of PDRM, i.e., the presence of a code for the adverse outcome and code(s) for the pattern of care that were consistent with one of the operational definitions adopted by the Delphi panel (see Appendix D). Because patients were enrolled an average of 1.32 years, the prevalence per year was 6.25%. Of those patients with a PDRM event detected, 685 (70.9%) had only one instance of PDRM, 199 (20.6%) had 2, and 82 (8.5%) had three or more

instances. Appendix G lists the number of events detected in the patient population for each consensus-approved definition of preventable drug-related morbidity.

A total of 1,359 total events were detected in the study population. Table 4.4 lists the 20 most common instances of preventable drug-related morbidity detected. The five most common definitions account for approximately 57% of PDRM events detected. The ten most common definitions detected 79.6% of events. Thus, 20% of the definitions account for about 80% of preventable drug-related morbidity detected in the study population.

The study population did not exhibit any instances of PDRM in 20 (approximately 40%) of the 49 consensus-approved definitions of preventable drug-related morbidity.

Pattern of Care and Outcome Measurement

The method employed to measure preventable drug-related morbidity in the patient population detected occurrences for each pattern of care and corresponding outcome independently. Appendix H lists the number of patients who had only the pattern of care, only the outcome, or both (thus PDRM) for each definition.

Outcomes were detected in a number of patients without the corresponding pattern of care present (thus, it was not an instance of PDRM as defined by the panel). Definitions 4 (Hmr/Hep- NoLab), 6 (Dep/Hx-Barb), 11 (Hmr/War-NSAID-INR), and 38 (Hmr/War-ABx-NoLab) had at least 500 patients with the outcome present, but 2 or fewer patterns of care detected. Three of the definitions (4, 11, and 38) detected bleeding as a common adverse outcome. This result indicates that the adverse outcomes were probably not caused by a preventable drug-related problem. Non-drug-related causes for adverse events in medical care are common (Brennan et al., 1991; Leape et al., 1991).

Table 4.4: Twenty Most Common PDRM Events Detected

Definition[a]	Mnemonic[b]	Instances of PDRM[c]	Percent of total PDRM[c]
45	CHF/Hx-ACEI	270	19.90%
33	CHF/Hx-Dig	184	13.50%
39	GI/NSAID	129	9.50%
22	Hypoth/Thy-T4TSH	103	7.60%
48	Asth/Hx-Bdilat-ICort	89	6.50%
19	CHF/Hx-NSAID	80	5.90%
5	GI/Hx-NSAID	63	4.60%
1	Dep/Hx-Benzo	56	4.10%
25	COPD/Hx-BB	54	4.00%
36	MI/Hx-ASA-BB	54	4.00%
20	HypoK/Kwd-NoK-Elec	44	3.20%
44	FB/SedHyp	42	3.10%
32	GI/Hx-OCort	38	2.80%
47	CHF/Hx-AArhy	37	2.70%
7	Dep/Hx-Symp	35	2.60%
16	ARsF/COPD-Benzo	19	1.40%
41	Dep/Hx-BB	15	1.10%
28	HyprK/ACEI-EleCBC	14	1.00%
8	Seiz/Antconv-DrugLvl	10	0.70%
49	FB/TCA	8	0.60%

[a]Definition number matches Appendix D
[b]Mnemonics are in Appendix E and F
[c]PDRM: preventable drug-related morbidity

There were several definitions for which a large number of patients had the pattern of care detected without the corresponding outcome present. Definitions 10 (Hyprth/Thy-T4TSH), 28 (HyprK/ACEI-EleCBC), 34 (ARnF/ACEI-BUNCr), 46 (ARnF/NSAID-BUNCr), and 49 (FB/TCA) were the most common definitions where patients had only the pattern of care detected. Four of those definitions (10, 28, 34, and 46) had some form of laboratory monitoring requirement. Two definitions (28 and 34) involve the use of ACE inhibitors with laboratory monitoring.

There were nine definitions for which the majority of the patients with a pattern of care present also had the corresponding outcome. Definitions 1 (Dep/Hx-Benzo), 5 (GI/Hx-NSAID), 7 (Dep/Hx-Symp), 25 (COPD/Hx-BB), 32 (GI/Hx-OCort), and 48 (Asth/Hx-Bdilat-ICort) are examples. These definitions will be discussed later as they relate to the Process-To-Outcome Value.

Days Between Pattern of Care and Outcome

In each instance of preventable drug-related morbidity, the number of days between the pattern of care and the corresponding outcome was determined. This is referred to as the Number of Days between the Pattern of care and Outcome (NDPO) (see Chapter 3). The average NDPO and standard deviation for all definitions with at least 10 detected instances are listed in Table 4.5.

The average NDPO per definition for a PDRM event to occur ranged from 18.81-203.50 (overall average of 130.06). Six of the 10 definitions with the longest average number of days between the pattern of care and the outcome had a laboratory monitoring requirement. Conversely, only two of the 10 preventable drug-related morbidity events with the shortest average NDPO had a requirement for laboratory monitoring. Thus, the

monitoring of laboratory results may allow the practitioner added time to recognize a potential drug therapy problem and prevent the adverse outcome from occurring.

Adjusted Days for Preventable Drug-Related Morbidity

Patients with only the pattern of care had the number of days between its occurrence and the end of the study period (September 30, 1999) calculated. Due to the truncation of the data collection period at 18 months, some of the patterns of care might have resulted in an adverse outcome if adequate time had been allowed. Thus, the data for actual PDRM events were used to determine a 95% cut-off point where most patterns of care could be expected to result in the corresponding adverse outcome. Those patterns of care within the 95% cut-off limits were not considered in the calculation of the Process-To-Outcome Value. If all patterns of care were used, regardless of time that had passed since its appearance, the PTOV would be biased downward.

The distribution of the NDPO for the 19 consensus-approved definitions with ten or more instances was reviewed. The distributions were not normally distributed. Therefore, mean plus 1.645 standard deviations did not appear to be an appropriate estimate of the 95% cumulative frequency cut-off point. Two other methods were used instead. Linear interpolation of the observed cumulative frequency distribution was used to calculate the 95% cut-off point for definitions 1 (Dep/Hx-Benzo), 5 (GI/Hx-NSAID), 7 (Dep/Hx-Symp), 16 (ARsF/COPD-Benzo), 19 (CHF/Hx-NSAID), 20 (HypoK/Kwd-NoK-Elec), 25 (COPD/Hx-BB), 32 (GI/Hx-Ocort), 33 (CHF/Hx-Dig), 36 (MI/Hx-ASA-BB), 41 (Dep/Hx-BB), 45 (CHF/Hx-ACEI), 47 (CHF/Hx-AArhy) and 48 (Asth/Hx-Bdilat-ICort). Because the data for definitions 8 (Seiz/Antconv-DrugLvl), 22 (Hypoth/Thy-T4TSH), 28 (HyprK/ACEI-EleCBC), 39 (GI/NSAID), and 44 (FB/SedHyp) were highly right-skewed, we chose to use the cumulative exponential distribution.

Table 4.5: Average Number of Days Between Pattern of Care and Outcome (NDPO)

Definition number[a] and mnemonic[b]	Number of PDRM[c] events detected	Mean number of days between pattern of care and the outcome	Standard deviation
1 (Dep/Hx-Benzo)	56	139.93	339.98
5 (GI/Hx-NSAID)	63	83.35	104.80
7 (Dep/Hx-Symp)	35	107.57	104.29
8 (Seiz/Antconv-DrugLvl)	10	142.00	74.61
16 (ARsF/COPD-Benzo)	19	133.84	116.89
17 (AUR/Hx-Antic)	4	114.75	130.34
19 (CHF/Hx-NSAID)	80	150.55	122.99
20 (HypoK/Kwd-NoK-Elec)	44	126.00	112.93
22 (Hypoth/Thy-T4TSH)	103	182.20	118.66
25 (COPD/Hx-BB)	54	115.93	133.64
28 (HyprK/ACEI-EleCBC)	14	199.50	118.02
32 (GI/Hx-Ocort)	38	88.95	102.37
33 (CHF/Hx-Dig)	184	150.65	122.76
35 (Hmr/War-INR)	3	69.33	47.17
36 (MI/Hx-ASA-BB)	54	18.81	38.44
39 (GI/NSAID)	129	171.62	118.82
41 (Dep/Hx-BB)	15	130.07	113.97
44 (FB/SedHyp)	42	192.38	111.45
45 (CHF/Hx-ACEI)	270	121.28	127.75
46 (ARnF/NSAID-BUNCr)	2	203.50	207.18
47 (CHF/Hx-AArhy)	37	131.35	112.22
48 (Asth/Hx-Bdilat-ICort)	89	161.03	132.85
49 (FB/TCA)	8	125.75	84.60

[a]Definition number matches Appendix D
[b]Mnemonic matches appendices E and F
[c]PDRM: preventable drug-related morbidity

Appendix I compares the 95% cut-off point (in days) for the two methods chosen (linear interpolation of the observed cumulative frequency distribution and the cumulative exponential distribution) with the cut-off point if the data were assumed to be normally distributed (mean plus 1.645 standard deviations). The comparison of the three estimated cut-off points demonstrates the variation due to the distribution of the data. In 14 of the 19 definitions, the estimates vary by more than 10 percent. Eleven of the 19 estimates demonstrated a difference greater than 20 percent.

The cumulative exponential distribution and the linear interpolation yielded similar results for several definitions, with 13 out of 19 having a difference of approximately 20% or less. Eight out of 19 definitions had differences less than 10% when comparing the two methods.

Patients With the Pattern of Care After Adjustment

There were 6,604 patterns of care detected in the patient population for the 19 definitions with 10 or more instances of PDRM. Of this total, 1,336 had the corresponding outcome present (thus, PDRM). After the 95% cut-off point was applied to each pattern of care, 4,138 patients with the pattern of care were included in the PTOV calculation. Appendix J lists the number of patients with each PDRM event, the number with only the pattern of care using no cut-off point, and the number of patients with the pattern of care after the 95% cut-off adjustment was applied. The number of patients eliminated who only had the pattern of care ranged from 0-675 per definition, with an average of 129.8.

Process-To-Outcome Value

A Process-To-Outcome Value (PTOV) was estimated for each definition with 10 or more instances of PDRM detected in the study population. The PTOV reflects the

proportion of patterns of care (after adjustment) in the population that resulted in the corresponding adverse outcome.

Table 4.6 lists the Process-To-Outcome Value for each definition with 10 or more instances of PDRM detected in the study population. The initial PTOV is based on all patients with the pattern of care prior to application of the 95% the cut-off adjustment. The adjusted Process-To-Outcome Value is based on the patterns of care remaining after the 95% cut-off values for each definition were applied.

The Process-To-Outcome Value for definitions with 10 or more instances of PDRM ranged from 0.04-1.00. Nearly half (9 of 19) of the definitions had a PTOV greater than 0.75. These definitions demonstrate a high association between the pattern of care and the adverse outcome detected in the database.

There were five definitions where the Process-To-Outcome Value was less than 0.25. These definitions contain a pattern of care that appears less likely to result in an adverse outcome.

Confirmatory Hypotheses

Risk Factors

MacKinnon's (1999) study identified risk factors associated with the presence of PDRM. These risk factors were used as confirmatory hypotheses in my study. Each risk factor was examined as an independent variable in a logistic regression model. All risk factors were significantly associated with the presence of preventable drug-related morbidity (Table 4.7).

All risk factors were entered simultaneously in a multivariate logistic regression model. In the multivariate model, gender and cardiovascular drugs were no longer significantly associated with the presence of PDRM. All other confirmatory risk factors

Table 4.6: PTOV Values Based on Various Cut-off Levels

Definition[a,b]	Initial PTOV[c]	Adjusted PTOV[d]
1 (Dep/Hx-Benzo)	0.98	1.00
5 (GI/Hx-NSAID)	0.98	0.98
7 (Dep/Hx-Symp)	1.00	1.00
8 (Seiz/Antconv-DrugLvl)	0.20	0.22
16 (ARsF/COPD-Benzo)	0.10	0.26
19 (CHF/Hx-NSAID)	0.09	0.37
20 (HypoK/Kwd-NoK-Elec)	0.06	0.11
22 (Hypoth/Thy-T4TSH)	0.37	0.45
25 (COPD/Hx-BB)	0.98	1.00
28 (HyprK/ACEI-EleCBC)	0.03	0.04
32 (GI/Hx-Ocort)	0.97	1.00
33 (CHF/Hx-Dig)	0.79	0.95
36 (MI/Hx-ASA-BB)	0.55	0.62
39 (GI/NSAID)	0.08	0.12
41 (Dep/Hx-BB)	0.94	1.00
44 (FB/SedHyp)	0.05	0.06
45 (CHF/Hx-ACEI)	0.47	0.75
47 (CHF/Hx-AArhy)	0.58	0.86
48 (Asth/Hx-Bdilat-ICort)	1.00	1.00
Average PTOV	0.54	0.62

[a]Definition number matches Appendix D
[b]Mnemonic matches appendices E and F
[c]Before cut-off adjustment
[d]After patterns of care eliminated based on cut-off point

Table 4.7: Confirmatory Risk Factors

Factor	Odds ratio	95% CI[a] for odds ratio	Sig.[b]
Gender	1.22	1.07-1.40	<0.004
Patients over 85	1.60	1.33-1.92	<0.0001
Number of prescribers	4.57	3.98-5.24	<0.0001
Number of drugs	5.98	5.21-6.85	<0.0001
Number of diagnoses	5.24	2.89-9.51	<0.0001
Cardiovascular drugs	6.74	5.36-8.47	<0.0001

[a]CI: confidence interval
[b]Sig: significance of odds ratio

were significant. Evidence of multicollinearity among the variables was examined. No two independent variables had a correlation above 0.3, with most 0.1 or less.

Resource Utilization and Cost

Resource utilization and costs were examined to determine if patients with preventable drug-related morbidity tended to use more resources and cost more than patients without an instance of PDRM. Based on the analysis, all categories examined were positively associated with the presence of preventable drug-related morbidity. Table 4.8 lists the average direct health care costs for patients with and without the presence of PDRM.

Table 4.8: Direct Health Care Costs

	Patients without PDRM	Patients with PDRM	Significance
Total direct costs	$3,423	$16,821	< 0.0001
Medical-related costs	$2696	$15,043	< 0.0001
Pharmacy-related costs	$446	$1,069	< 0.0001

NOTE: PDRM: preventable drug-related morbidity

In addition to direct medical expenses, patients with preventable drug-related morbidity tended to have more hospital admissions, visit the emergency room more often, go to the physician's office more often, and use more drugs than those patients with no instance of PDRM detected.

Root Cause Analysis

A root cause analysis was conducted to determine if the measure of preventable drug-related morbidity based on consensus-approved definitions could be used to identify systematic problems in quality of the medication use system. An expert panel of six health care professionals participated in the root cause analysis (Appendix C).

A quality consultant employed by the managed care organization facilitated the meeting. The principal investigator (RJF), a faculty member from the University of Florida, and a group interaction observer were also present at the meeting. The principal investigator (RJF) introduced the topic and described the information distributed to panel members. At that point, the quality consultant facilitated the root cause analysis.

The primary outcome of the meeting was a series of cause-and-effect diagrams (appendices K, L, M, and N). These diagrams list possible root causes identified by the panel for several consensus-approved definitions of preventable drug-related morbidity. A number of root causes were identified for each PDRM definition addressed by the panel. Possible root causes were grouped into 5 major categories: 1) the provider, 2) the insurer, 3) the patient, 4) the medication use process, and 5) other causes.

Dr. Barbara Brice observed group dynamics during the meeting and provided a written report (Appendix O). While consensus was not obtained due to time constraints for the meeting, the group interaction and results demonstrate the use of a PDRM measure as a quality improvement tool.

CHAPTER 5
DISCUSSION

Introduction

Chapter 5 will discuss the findings and implications of our study. First, the consensus-approved definitions and the voting patterns of the Delphi panel will be discussed, followed by the operationalization of the definitions and the measurement of preventable drug-related morbidity. The root cause analysis will be presented as it relates to the use of the measure. Additionally, the validity of the definitions will be addressed. Finally, concluding remarks will be offered along with the study's limitations, significance and implications for future research.

Geriatric Medicine Expert Panel

Replication of MacKinnon's Work

The Geriatric Medicine Expert Panel was convened to gain consensus on explicit definitions of preventable drug-related morbidity. The panel used MacKinnon's (1999) work as a starting point. MacKinnon (1999) used literature and the Delphi technique to define 52 explicit scenarios of preventable drug-related morbidity. Replicating MacKinnon's (1999) methodology strengthens validity of our explicit definitions by using a different expert panel to come to an independent conclusion about their relevance and representativeness.

The current study used the Delphi technique with three rounds to attain consensus. There was a high level of agreement after the third round, with 43 out of 49 (87.8%) definitions having either all 7, or 6 out of the 7 panel members agreeing it was

an instance of PDRM. No definition in the third survey received less than 71% (5 out of 7) of the panel agreeing it was an instance of PDRM.

MacKinnon's (1999) panel required two rounds to gain consensus. The difference in the number of rounds needed to gain consensus could be due to the fact that all MacKinnon's (1999) panel members practiced in the same location. The chief physician at this location also took an aggressive leadership role in the project. The current panel had more diverse practice settings. No two physicians were in the same group practice (although three were faculty members at the same university but practiced at different locations). The diversity of practice sites in the current panel demonstrates that definitions of preventable drug-related morbidity may have broad agreement among physicians.

Consensus-Approved Definitions

The Geriatric Medicine Expert Panel accepted 49 definitions of preventable drug-related morbidity (Appendix D), including 44 of the 52 definitions from MacKinnon's (1999) study. Panel members often cited literature and specific criteria to support their decision to either accept or reject a specific scenario. Thus, the panel demonstrated an evidence-based thought process, adding to the validity of out results (Craig et al., 2001; Rosenberg & Donald, 1995).

The panel accepted 2 of the three definitions rejected in MacKinnon's (1999) study. This result could call into question the validity of the definitions. However, both definitions had very specific laboratory monitoring requirements. MacKinnon's (1999) panel rejected these definitions because they disagreed with the length of time specified for laboratory monitoring, not the connection of pattern of care to outcome (personal

communication between the principal investigator (RJF) and MacKinnon. 2000). Thus, acceptance by the panel is not extraordinary.

The panel also suggested three additional definitions that were ultimately accepted. Other definitions were suggested that were either rejected by the panel or were not presented to the panel because I could not operationalize the definitions.

Evidence-Based Medicine and the Panel

Evidence-based medicine has been defined as "the process of systematically finding, appraising and using contemporaneous research findings as the basis for clinical decisions" (Rosenberg & Donald, 1995, p.1122). MacKinnon (1999) used the literature to develop each definition of preventable drug-related morbidity. New definitions also had to be supported by the literature. Thus, each definition was evidence-based.

The research method employed by MacKinnon (1999) and the current study directed panel members to operate in a manner consistent with the definition of evidence-based medicine offered by Rosenberg and Donald (1995). Panel members were given definitions that were developed based on the literature, then used their knowledge of the evidence and their practice patterns to accept or reject the definitions. Thus, there is interplay between evidence and practice. This methodology is offered in contrast to the use of expert opinion with no direct citation of evidence for support (otherwise referred to as implicit judgement).

Implicit judgement has demonstrated a wide variability and may produce invalid results because experts do not agree. Our study may offer a baseline for expert agreement when presented with evidence.

Panel Developed Explicit Definitions Versus Implicit Judgement

Broad agreement between MacKinnon's (1999) panel and the current study was demonstrated. The differences that exist are expected when relying on the interplay between evidence and clinical judgement. Differences may be traced to new evidence between the time the two panels convened and practice pattern variation. The results suggest that the development of evidence-based, explicit definitions for PDRM can be accomplished with practicing physicians.

Explicit definitions are offered as an alternative to implicit or structured implicit methodologies commonly used to determine if an adverse drug event occurred. Implicit evaluation suffers from a lack of reliability (Allison et al., 2000; Ashton et al., 1999; Brennan, 2000). Thus, practice pattern variation may play a larger role in the assessment of each clinical scenario. Therefore, while the current study and MacKinnon's (1999) panel may not have perfect agreement, once the definitions are applied to the data, a consistent measure is afforded.

The Panel and Preventability Framework

Panel members were instructed to use Hepler and Strand's (1990) framework to determining whether events were preventable or not. An adverse outcome attributable to drug therapy was deemed preventable if; (1) the adverse outcome was preceded by a *recognizable* drug therapy problem, (2) the adverse outcome of the drug therapy problem had been reasonably *foreseeable*, (3) the cause of the adverse outcome could have been *identifiable* with reasonable probability, and (4) the cause of the adverse outcome could have been reasonably *controllable* within the context and objectives of therapy.

Written responses from panel members demonstrated their use of this framework in their assessment of each definition. Several selected statements made by panel

members (both for and against the event's preventability) and their context are detailed below for each component of the preventability framework.

- "Inappropriate treatment for condition." Referring to use of long-acting benzodiazepines in patients with a history of depression. (Recognizable)
- "Unusual occurrence with short term antibiotics. Usually occurs later." Referring to the use of antibiotics with warfarin. (Recognizable)
- "Well accepted use of agents these days." Referring to the use of aspirin and beta-blockers to prevent a secondary myocardial infarction. (Recognizable)
- "Would not use if prior history of GI bleeding." Referring to the use of oral corticosteroids in a patient with a history of GI problems. (Recognizable)
- "Beta-blockers mask hypoglycemic levels." Referring to use of beta-blockers in diabetic patients. (Recognizable)
- "Recognizable as long as we know exactly what they are taking. Often we don't." Referring to the use of NSAIDS and their availability over-the-counter. (Recognizable)
- "HbA_1C is recommended every 3 months for IDDM and every 6 months for NDDM. But this will not predict acute changes (hyperglycemia); for this, daily glucose fingersticks are better." (Foreseeable)
- "HbA_1C should be substituted with daily blood sugars." (Foreseeable)
- "Not necessarily related. Other factors may be at work." When discussing falls and tricyclic antidepressants. (Identifiable)
- "Not a strong correlation." When discussing falls and the use of nitrates. (Identifiable)
- "Digoxin with therapeutic levels can cause bradycardia." Referring to use of digoxin in a CHF patient with heart block or advanced heart block. (Identifiable)
- In referring to the use of NSAIDs, one physician stated that "patients often take these on their own (OTC)." (Controllable)
- "NSAID usage can cause GI problems even with cytoprotective agents." (Controllable)

- "Patients fall and break their hips without being caused by tricyclic antidepressants." (Controllable)
- "COX-2 agents are better alternative to NSAIDs to prevent GI problems." (Controllable)
- "Avoid tricyclics in the elderly." (Controllable)

Operationalization

The gold standard in the identification of medical codes in an administrative database is the use of experienced medical record coders combined with a physician (Steinberg et al., 1990). Our study used that methodology to identify all possible codes for explicit definitions of preventable drug-related morbidity.

Operationalization of the medical care components for each definition involved the use of experts in the application of ICD-9 and CPT codes. Two medical record coders were instructed to identify all possible codes for the pattern of care and outcome for each consensus-approved definition. An intermediate list of codes was generated using all codes identified by at least one coder.

The intermediate list of codes was given to a physician for review with instructions to determine the clinical relevance of the code to the definition. The physician reviewer eliminated nearly 20% of the codes identified by the medical record coders. The number of codes eliminated through the physician review suggests that asking coders to think clinically exceeded their capabilities. The use of a physician to review codes was critical to the reliability of selecting appropriate codes.

Measurement

Prevalence of Preventable Drug-Related Morbidity

Out of 11,711 patients eligible for the study, 966 (8.2%) had at least one instance of preventable drug-related morbidity. This number is higher than MacKinnon's (1999)

prevalence of 2.9%. The first thing to consider is whether the length of the data collection period was the cause for the difference. MacKinnon (1999) collected data over a 12 months period. The current study allowed for up to 18 months of data collection. The average patient in the current study was enrolled in the managed care plan for 483 days. This is 1.32 times longer than MacKinnon's (1999) study period. The current study yielded a PDRM prevalence rate of 6.2% per-member-year, which is still more than double MacKinnon's (1999) rate.

A second possible explanation for the higher prevalence is the process used to identify medical claims codes. In MacKinnon's (1999) study, the principal investigator (NJM) chose medical claims codes with no outside expertise. The current study used experienced medical record coders and a physician to identify all possible codes. Thus, it is likely that a more complete list of ICD-9 and CPT codes was available.

A third possible explanation is a difference in study populations. MacKinnon (1999) does not provide demographic data on his population; thus comparison is not possible. Both studies, however, focus on the elderly.

Comparison of PDRM Detection With MacKinnon's Study

Of the 966 patients with preventable drug-related morbidity, 70.9% had only one instance and 29.1% had more then one instance of PDRM. These numbers are similar to MacKinnon's (1999) study where 62.9% had only one instance of preventable drug-related morbidity and 37.1% had more than one. Thus, the study populations demonstrated a similar distribution of events. This may suggest that a more reliable coding process increased the identification of PDRM events.

The detection of specific preventable drug-related morbidity in our study population and MacKinnon's (1999) population illustrates both important similarities and

differences. Appendices P and Q list the most common PDRM events detected in each population. Four of the most common events were similar in both studies. Two of the four definitions common to both study populations had congestive heart failure (CHF) as their adverse outcome of interest (definition 19-CHF/Hx-NSAID, and definition 45-CHF/Hx-ACEI). Thus, both study populations exhibit problems with the patterns of care patients with CHF receive. Congestive heart failure is the most common discharge diagnosis by diagnosis-related groups (DRG) in the United States, accounting for 1 million hospitalizations and 200,000 deaths per year (Costantini et al., 2001). Given the prevalence of CHF and the poor treatment patterns, detection of PDRM involving these patients adds validity to our measure (McDermott et al., 1998; Reis et al., 1997; Stafford et al., 1997).

The event most evenly detected PDRM event in both study populations had hypothyroidism as the adverse outcome (definition 22, Hypoth/Thy-T4TSH). In both study populations, the event accounted for 7.6% of total PDRM events detected. The medical director of the managed care organization initially questioned this result. However, the similarity of the results between patient populations added to the validity of the result.

A patient experiencing a secondary myocardial infarction (MI) without receiving either aspirin or a beta-blocker was also common to both study populations. This is a widely accepted pattern of care and should prompt practitioners to review all patients with a previous MI to evaluate the pattern of care. However, aspirin use is difficult to detect in an administrative database due to its over-the-counter (OTC) status. Thus, both studies may have patients with an appropriate pattern of care based on the consensus-

approved definition. Patients may be receiving aspirin, yet still have a secondary myocardial infarction, indicating that beta-blockers may be of more importance in preventing secondary myocardial infarctions.

The current Geriatric Medicine Expert panel rejected four of the top 12 definitions in MacKinnon's (1999) population. If these specific scenarios had been measured in the current study, the actual difference in the detection of events may have been greater.

Definitions With No Events Screened Positive

The study population did not exhibit any instances of preventable drug-related morbidity for 20 (40.8%) of the 49 consensus-approved definitions. This number is similar to MacKinnon's (1999) study where 23 out of 52 (44.2%) definitions detected no instances of preventable drug-related morbidity.

Four consensus-approved definitions with no instances of PDRM detected in the study population identified specific drug toxicities (theophylline, anticonvulsants, lithium, and aminoglycosides). The lack of detection may be in part a better job of monitoring for the effects of these medications and preventing drug-related morbidity. The lack of events may also be due to the difficulty of detecting these outcomes in an administrative database. Signs and symptoms associated with drug toxicity often go unrecognized or are not coded as such. There are "e-codes" which identify adverse events related to the use of a medication, but rarely are these codes used (Banks et al., 1999; Bero et al., 1991).

Major or minor hemorrhagic events due to the misuse of heparin or warfarin were also rare in the current population. The use of these agents has raised serious safety concerns in the literature for years. The evidence from this study may lead us to

conclude that the health care system has reduced the prevalence of these specific drug-related morbidity events.

Renal failure was not a common PDRM event detected in this patient population. Renal dosing of medications and the renal monitoring of elderly patients is strongly recommended (DiPiro et al., 1999). Once again, the results suggest that these patterns of care have been improved in the current medication use system.

Pattern of Care and Outcome Assessment

Previous studies have looked at process indicator identification using computer databases (Classen et al., 1999; Raschke et al., 1998). However, these studies only look for a poor process without identifying the corresponding adverse outcome. The strength of the current study is the linking of the pattern of care with the corresponding outcome. Each pattern of care and corresponding outcome was identified independently in the administrative database. A date of occurrence was attached to each component. Patients with both components present (thus, PDRM) had the Number of Days from Pattern of care to Outcome (NDPO) recorded. Patients with the pattern of care present but no corresponding outcome also had the number of days between its presence and the end of the study period (September 30, 1999) calculated.

Preventing adverse outcomes requires that practitioners have sufficient time between the presence of the pattern of care and the outcome to avert the adverse event. Using the framework for preventability established earlier, a practitioner must recognize the drug-related problem and foresee the potential for a negative outcome. Additionally, the practitioner must have adequate time to identify and control the cause within the normal course of care. Thus, the time between the pattern of care and outcome is a useful measure. However, no attempt was made to make a clinical judgment about how long

the length of time between the pattern of care and outcome could, or should, be before it should not be counted as a PDRM event.

There was a large variability in the amount of time for a pattern of care to result in an adverse outcome. An adjustment in the number of patients with only the pattern of care was made to account for patterns of care that did not have sufficient time to result in the adverse outcome (see Chapter 3).

Process-To-Outcome Value

The Process-To-Outcome Value (PTOV) reflects the proportion of patients with a pattern of care (after adjustment) that also had the corresponding outcome. Definitions with a high Process-To-Outcome Value demonstrate a high association between the presence of the pattern of care and the adverse outcome. Each definition with a high PTOV has the potential to serve as an indicator in the medication use process.

Appendix R lists the Process-To-Outcome Values for each definition where at least 10 instances of PDRM were detected. Six of the consensus-approved definitions (1-Dep/Hx-Benzo, 7-Dep/Hx-Symp, 25-COPD/Hx-BB, 32-GI/Hx-OCort, 41-Dep/Hx-BB, 48-Asth/Hx-Bdilat-ICort) had a Process-To-Outcome Value of 1.00 (refer to Appendix D for numbers and appendices E and F for mnemonics). This means that all patterns of care (after adjustment) eventually resulted in the adverse outcome.

Three of the six definitions with a PTOV of 1.00 had a pattern of care that included a previous history of depression. Thus, patients with a diagnosis of depression warrant increased attention by health care practitioners. Indicators that identify patients with depression and the corresponding drug-related problems should be developed based on the results of this study.

The most common preventable drug-related morbidity event with a PTOV of 1.00 involved patients with a history of asthma who are not on an inhaled corticosteroid, but are receiving a bronchodilator (89 events detected in the patient population). Treatment guidelines for asthma patients clearly call for inhaled corticosteroids as preventative therapy (DiPiro et al., 1999). This study demonstrates that patients who do not receive inhaled corticosteroids will inevitably have an adverse outcome that could have been prevented. The use of inhaled corticosteroids is recommended as an indicator of quality in the medication use system. This excessive use of bronchodilators may also serve as an indicator of poorly controlled asthma patients.

The definition including asthma as the adverse outcome illustrates the issue of evidence versus practice patterns. While the definition had a PTOV of 1.00, it only received minimal agreement in the Delphi panel (5 out of 7 panel members). Thus, even in a process where evidence was used to develop explicit definitions and panel members were given instructions on a framework for the process, subjective practice pattern variation is still evident. This result makes public the decision process physicians face when prescribing medications for their patients.

There were other consensus-approved definitions where the Process-To-Outcome-Value was relatively high, although not 1.00. These patterns of care may also prove useful as indicators of poor medication use. Definition 33 (CHF/Hx-Dig) resulted in 184 adverse outcomes from 193 patterns of care (PTOV = 0.95). This pattern of care would also be a good indicator of quality in the medication use system.

Patients with a history of congestive heart failure who were not receiving an ACE inhibitor (definition number 45) resulted in the most instances of preventable drug-related

morbidity in our patient population (270). This pattern of care also had a relatively high PTOV (0.75). The use of an ACE inhibitor is well accepted for most patients with CHF. However, one study demonstrated that only 18% of CHF patients discharged from the hospital received appropriate ACE inhibitor therapy (McDermott et al., 1998). Other studies indicate that ACI inhibitors are underutilized in the treatment of CHF (Reis et al., 1997; Stafford et al., 1997).

Combined with definition 33 (CHF/Hx-Dig), patients with congestive heart failure should receive additional attention regarding their medication use in order to prevent adverse outcomes from occurring. Added attention could result in significant reductions in hospitalizations, since congestive heart failure is the most common DRG discharge diagnosis and adverse events related to ACE inhibitors are a common reason for admission (Costantini et al., 2001; Darchy et al., 1999). Programs targeted at CHF patients could reduce the per-patient cost of care and improve patient outcomes (Fonarow et al., 1997).

Definitions With a Low PTOV

Several consensus-approved definitions had a number of patients with the pattern of care present but not the corresponding outcome, even after adjustment for NDPO. Thus, these definitions had a low PTOV. The five definitions with the most patterns of care and their PTOV are listed in Table 5.1.

Each of these medication use issues represents a common treatment regimen. The presence of a low PTOV suggests that the pattern of care is not strongly associated with the negative outcome. However, they still may be of value as an indicator if they are of high cost, high volume, or high risk.

One definition that may serve as an indicator due to its relatively high frequency is number 39 (GI/NSAID). There were 129 patients who were on 2 or more NSAIDS for more than 2 weeks with the corresponding outcome of gastritis and/or upper GI bleed and/or GI perforation and/or GI ulcer and anemia. While the association between the pattern of care and the adverse outcome was not strong (PTOV = 0.12), the sheer number of patients with this pattern of care warrants attention. This is supported by literature that implicates non-steroidal anti-inflammatory drugs (NSAIDs) as a leading cause of drug-related hospital admissions (Cunningham et al., 1997).

Table 5.1: Preventable Drug-Related Morbidity Definitions With a Low PTOV

Definition[a]	Mnemonic[b]	Number of patterns of care-only	Number of PDRM[c] events detected	PTOV[d]
39	GI/NSAID	929	129	0.12
44	FB/SedHyp	655	42	0.06
20	HypoK/Kwd-NoK-Elec	365	44	0.11
28	HyprK/ACEI-EleCBC	360	14	0.04
19	CHF/Hx-NSAID	139	80	.37

[a]Definition number matches Appendix D
[b]Mnemonics in appendices E and F
[c]PDRM: preventable drug-related morbidity
[d]PTOV: process-To-Outcome Value

Preventable Drug-Related Morbidity as an Extension of Drug Use Evaluation

Drug use evaluation (DUE) has been used in health care to determine the appropriateness of medication use. However, most DUE programs focus on prescribing, rather than viewing the entire system of medication use. Beers et al. (1991) attempted to develop explicit criteria to evaluate inappropriate medication use in nursing home patients. Beers (1997) later update the criteria to look at all elderly patients, rather than just the frail in nursing homes. Each set of criteria identified medications that should be

avoided in elderly patients with certain conditions, and doses, frequencies, or durations of therapy that should not be exceeded in the elderly. In both cases, the authors provide explicit criteria that evaluate only prescribing, rather than the use of medications. Additionally, the lack of clinical information made the assessment of appropriateness questionable at best. In most cases, one cannot state unequivocally that a drug should not be used without consideration of other factors.

Hanlon et al. (1992) also developed explicit criteria to evaluate the use of medications, called the Medication Appropriateness Index (MAI). The index is based on 10 factors to assess the appropriateness of medication use (Hanlon et al., 1992). Their work was an important advancement over previous studies because they attempted to assess factors other than prescribing the right drug. They gathered limited clinical information to assist in their determination of appropriate use. However, they did not address ongoing monitoring or the outcomes of the medication use.

The current study advances previous methods for drug use evaluation in that it assesses medication use, not just prescribing, and the outcome of care. Beers (1997) makes the point that clinical information should be used to judge appropriateness. Our study does this by looking for laboratory requirements or a past medical history where indicated. The use of laboratory monitoring also advances the Medication Appropriateness Index from Hanlon et al. (1992).

The linking of an outcome with the pattern of care is the most significant advancement in drug use evaluation offered by this study. Buetow et al. (1997) suggest that inappropriate prescribing is related to the outcome of medication use and not the process. By linking the outcome and the pattern of care, true inappropriate drug use can

be assessed. The study also assessed the association of poor patterns of care and the appearance of adverse outcomes. The results of the study should focus attention on more clinically relevant issues.

Validity of a Measure of Preventable Drug-Related Morbidity

Validity of the measure of preventable drug-related morbidity is supported by much of the data previously presented. However, additional evidence will be discussed using Messick's validity framework (Messick, 1989). Messick treats validity as a unitary concept with both an evidentiary and consequential basis for the interpretation and use of a measure (Messick, 1989).

Evidentiary Basis for Interpretation

The first quadrant in Messick's framework addresses the evidence gathered to support the interpretation of our measure. The evidence needed for interpretation addresses construct validity with support from content or face validity.

Face and content validity

The expert panel defining preventable drug-related morbidity supports the evidential basis for interpretation. Panel members came to agreement on 49 explicit definitions of PDRM. Thus, the panel agreed that the definitions were relevant to the issue of preventable drug-related morbidity and were useful in detecting instances of PDRM. The current panel's results add to the evidence from MacKinnon's (1999) content panel.

Validity is also supported by the panel member's use of literature in their decision process. Evidence-based medicine uses the literature systematically to make clinical decisions (Mootonen et al., 2001; Rosenberg & Donald, 1995). The use of evidence in

the process supports validity of the definitions as being relevant to preventable drug-related morbidity.

The panel also recommended additional definitions that were accepted, adding to the representativeness of the test. By recommending additional definitions, the panel was reasoning within the framework of the study and using their expertise to identify additional instances of preventable drug-related morbidity.

Risk factors

Association with known risk factors also supports the validity of the measure of preventable drug-related morbidity. The current study used MacKinnon's (1999) risk factors as confirmatory hypotheses to support the use of preventable drug-related morbidity definitions. Using a simple logistic regression model, all factors were independently associated with the presence of preventable drug-related morbidity. This mirrored the results of the MacKinnon (1999) study.

The intent of the study was not to determine the causative direction for these confirmatory hypotheses. Rather, it was important to show that patients with 4 or more prescribers, 6 or more prescriptions, 4 or more diagnoses, etc., were more likely to have an instance of preventable drug-related morbidity detected. The strong association of the presence of a hypothesized risk factor and preventable drug-related morbidity adds to our ability to interpret the measure.

Resource use

The patient population was studied to determine if a relationship between the amount of resources used and the presence of preventable drug-related morbidity existed. As the case with confirmatory risk factors, the exploration of costs adds evidence for the interpretation of a measure of PDRM. Theoretically, patients with preventable drug-

related morbidity should use more resources than patients who have not experienced an adverse event.

Patients with preventable drug-related morbidity experienced more hospitalizations than patients without PDRM. There are a number of studies that demonstrate that a significant number of patients are admitted to the hospital as a result of drug-related events (Bergman & Wiholm, 1981; Bero et al., 1991; Bigby et al., 1987; Cunningham et al., 1997; Darchy et al., 1999; Hallas et al., 1992). While the intent was not to determine causative direction, evidence supports the proper association.

Patients with preventable drug-related morbidity tended to use other health care resources (emergency room visits, physician office visits, and medications) more often than those with no evidence of PDRM. This has been postulated and studied by other authors (Bates et al., 1997; Bootman et al., 1997; Dennehy et al., 1996; Johnson & Bootman, 1995; Tafreshi et al., 1999). Again, the direction of causation was not determined. However, showing the association between patients with PDRM and the use of additional resources adds to the evidence for validity.

Overall, the cost of caring for patients with preventable drug-related morbidity was higher than those without PDRM. This was true from the payer's perspective, the patient's viewpoint, and for total direct health care costs. The direction of causation once again was not determined. Other studies have shown that patients with PDRM have a higher total cost than those without (Bates et al., 1997; Classen et al., 1999; Thomas et al., 1999).

Evidential Basis for Use

The discussion regarding the evidence for interpretation of the measure of PDRM may also be applied to the use of the measurement. Thus, the expert panel and

measurement in the patient population support validity for use as a measure of PDRM. In addition to this, the relevance and utility of a measure are explored through a root cause analysis.

Root cause analysis

The results from the root cause analysis help to explore the relevance and utility of the measure of preventable drug-related morbidity as it relates to quality of the medication use system. The root cause analysis is an important tool in quality assessment and improvement initiatives (Bates, 1996; Fernandes et al., 1997; JCAHO, 1996; JCAHO, 1998; Shinn, 2000). A root cause analysis is often used in a systematic process to uncover quality problems in medication use.

Quality assessment and improvement is an important function in health care (JCAHO, 1996; JCAHO, 1998). The acronym FOCUS-PDCA was developed by the Columbia/HCA Corporation in Nashville, Tennessee to provide a systematic framework for quality assessment and improvement activities (Gerard & Arnold, 1996; Redick, 1999). The use of the measure of preventable drug-related morbidity in a systematic framework such as FOCUS-PDCA was accomplished. The FOCUS-PDCA process is reviewed along with the study components.

- **F**ind a process to improve: In the study, a measurement of PDRM provided prevalence estimates of patterns of care that resulted in adverse outcomes. The measure served as an indicator that identified potential improvement opportunities.

- **O**rganize a team that understands the process: A panel of physicians and pharmacists involved in ambulatory care of elderly patients was convened to address quality issues.

- **C**larify current knowledge of the system: The root cause analysis panel did not formally flow chart the medication use process. However, there was discussion on the flow of patient care in the current system.

- **U**nderstand the causes of variation: The root cause analysis panel developed cause-and-effect diagrams for the most prevalent PDRM events (Appendices K, L, M, and N). Determining the relative importance of each cause was beyond the scope of our study.

- **S**elect the process improvement of intervention: Several potential system improvements were suggested at the root cause analysis meeting. However, this and all remaining steps in the FOCUS-PDCA process were beyond the scope of our study.

- **P**lan the improvement.

- **D**o implement the improvement.

- **C**heck the improvement by gathering and analyzing data.

- **A**ct on the data to hold the gain or continue improving.

While the process employed in the study did not allow time for the root cause analysis panel to come to full consensus, there was ample evidence to demonstrate that the measure of preventable drug-related morbidity was useful in identifying quality problems in the medication use system. This demonstrates their relevance and utility to identify performance improvement opportunities.

Representatives from the managed care partner are exploring possible interventions to reduce the problem of PDRM in their patient population using the measure and results of the root cause analysis. This further supports the utility of a measure of preventable drug-related morbidity to improve medication use.

Consequential Basis for Interpretation

While a direct measure of the consequential basis for interpretation of our results was not planned as part of the study, some important points can be made. The consequential basis for interpretation of the measure of PDRM assesses the value associated with the label. In terms of preventable drug-related morbidity, the key word

may be *preventable*. By implying that an outcome was preventable, a negative value is attached if the event occurs. The root cause analysis panel discussed quality issues involved with the definitions and what the measure would mean to the MCO. In particular, poor quality and a system that is not safe could be implied. Also implied is that an error may have occurred that the physician is responsible for due to his decision making (Bates et al., 1995a). These would certainly have implications for the consequences of interpreting a measure of PDRM.

Consequential Basis for Use

The consequential basis for use addresses the social consequences of the measure. Once again, no direct measure was planned to assess this dimension of validity. However, the physician who was disqualified from the Delphi panel obviously was concerned about social consequences based on the summative use of the measure (the measure is intended for formative purposes, i.e., quality improvement, and not for judging individual cases or practitioners). This physician's concern was centered on the use of the measure to judge individual practitioner's care patterns. Recall that he said, "I don't care what you say these definitions will be used for, I know that *[MCO name]* will use them as practice standards and tell me I am not doing things right." He was concerned about the consequences of the summative use of a PDRM measure on his practice. This use should be acknowledged as one possible use if the measure is released for broader application.

Potential social consequences could also be seen at the organizational level if the measures are used in a summative, rather than formative, manner. The use of a measure of preventable drug-related morbidity in report cards to assess the quality of care provided by an organization could have consequences for social policy if they were used

for summative purposes. The consequences would stem from public and payer reaction to the information. Organizations with a lower measure would benefit from the release of such information. However, those organizations with a poor measure would risk losing their business. The measure was not designed for this purpose, however it must be recognized as a potential consequence.

Conclusion

This study began with four research objectives. The first was to develop and validate definitions of PDRM. This research objective was accomplished through a Delphi panel that replicated MacKinnon's (1999) work. The Delphi panel approved 49 explicit definitions of preventable drug-related morbidity. These definitions were judged to be both relevant and representative of the domain of preventable drug-related morbidity.

The second research objective was to identify issues in operationalizing the definitions of PDRM to be used in a computer database. Two medical record coders and a physician were used to generate ICD-9 and CPT codes relevant to each PDRM definition. The physician was a critical component in accomplishing this objective due to variation in selecting codes. Nearly 20% of the codes selected by medical record coders were eliminated through a clinical review.

The third objective was to use the explicit definitions to measure PDRM in the study population. A total of 966 (8.2%) patients had at least one instance of preventable drug-related morbidity identified. Because the patients were in the study for more then one year, a prevalence rate of 6.25% was calculated. The number of patients with PDRM detected using explicit definitions is impressive. The result lends credibility to the

methodology used to develop explicit definitions for preventable drug-related morbidity and their application to a managed care organization's database.

The measurement of PDRM in the population provided a wealth of information on the associations between the pattern of care and the corresponding outcome. Each occurrence of a pattern of care and outcome was identified independently. This allowed the assessment of patients with either component of the definition or both components (defined as PDRM). The percentage of patients with the pattern of care that also had the corresponding outcome detected was used as an estimate of association. The study identified specific instances of preventable drug-related morbidity where the pattern of care inevitably resulted in the corresponding adverse outcome.

The final research objective sought to explore the use the measure of PDRM in a structured quality assessment and improvement process to identify potential problems in the medication use system. This was accomplished through a panel that performed a root cause analysis when presented with the ten most common definitions. The panel generated cause-and-effect diagrams that can be used to drive improvement opportunities. The panel did recommend potential improvement programs.

The study is important in the developing research areas of explicit criteria and database research. The methodology employed to identify both the pattern of care and the corresponding outcome is a significant improvement over previously published work. The definitions identified a broader range of patient data that can be used to assess medication use beyond prescribing. Thus, these may be used as indicators of potential problems in the medication use system. These indicators may be used at the health plan

level in terms of benchmarking and quality improvement. However, their ultimate use may be as targeted interventions in direct patient care.

Potential Limitations

Despite a literature review and the use of an expert panel, the 49 definitions represent only a portion of the PDRM events that occur. There is no way of knowing the proportion of the domain that has been captured. However, two content panels should have identified the most common events. Additional work and literature review will be necessary to add to the definitions. However, a prevalence rate of 6.2% is a fairly sizable figure, suggesting the most common PDRM events were identified.

As with any research on an administrative database, the results are only as good as the data. There are many problems when relying on ICD-9 and CPT codes, such as undercoding, overcoding, misspecification and missequencing (Romano & Luft, 1992). The data given by the managed care partner was used as received. The data were viewed for cleanliness by searching for duplicate visit information and viewing data entry for consistency. As this type of research gains in popularity, the data quality will also improve.

Our study population may not be representative of the elderly in America, thus generalizability is an issue. The study also only looks at the elderly. The question of other age groups (particularly pediatric patients) should be explored in future studies.

There are limitations in determining of the link between the pattern of care and outcome in each patient with an event. The correlation between the variables is probably not one-to-one. We do not know the sensitivity of the data. However, the results may provide an estimate of specificity as a lower bound estimate. This does provide fertile ground for future studies to look at these issues and determine their predictive ability.

The study did not attempt to determine a reasonable amount of time between the pattern of care and the outcome. This could be a limitation to our Process-To-Outcome Value. In health care, if one waits long enough, the outcome will eventually occur. I chose not to use clinical judgment to determine how long was long enough for each definition. Thus, there are pattern to outcome intervals in the study that might have been too long and do not appear to make clinical sense. However, other cases that had a large number of days between the pattern of care and the outcome are appropriate. One example is definition 5 (GI/Hx-NSAID) where the appearance of anemia may take a long time in many patients with a slow GI bleed.

It is important to recognize that the measure of preventable drug-related morbidity based on the consensus-approved definitions was intended for use at a population level to identify opportunities to improve the quality of the medication use system. By itself, the measure does not address whether an organization is doing well or poorly. It is meant to gather information and to be used in a formative manner. Likewise, the measure was not meant to evaluate the care patterns of individual practitioners, especially not for punitive purposes. If the definitions are used in a summative manner, their acceptance by health care organizations and practitioners could be limited.

The definitions are not meant to serve as rigid guidelines for care. For example, the definition addressing the use of an ACE inhibitor in patients with congestive heart failure does not recommend that every patient receive the drug. However, it does signal an area to evaluate clinically to determine if the agent is indicated. Thus, they could be used to improve the care of individual patients by targeting patterns of care for additional attention.

The root cause analysis process did tot prioritizing the system issues identified in the session. They did not selecting improvement opportunities either. This may limit my conclusions a regarding the use of the measure of PDRM. The most important issues would lead to program implementation and impact assessment.

Significance of Study

The primary significance of our study is the further development of explicit definitions for preventable drug-related morbidity. By adding to MacKinnon's (1999) study, more evidence is gathered in support of the use of explicit definitions to measure preventable drug-related morbidity. Using a different expert panel strengthens the face and content validity of the definitions. The measurement adds to evidence by using a different patient population.

The current study expanded on previous work by MacKinnon (1999) in the operationalization of the definitions. The current study used a rigorous process to identify a broader range of acceptable codes that can be replicated. A computer program was designed to automatically search an administrative database for preventable drug-related morbidity. Thus, my measure is more reliable.

The study makes an important contribution to the literature by linking medication use with other clinical components (such as laboratory monitoring) and assessing its association with the outcome. Most previous studies only view the process of care without consideration of the outcome.

The study adds to sparse information available on PDRM occurring across the continuum of care. Much of the work done on adverse drug events has been in or around organized health care settings (such as a hospital). Ambulatory care accounts for a

significant portion of patient encounters and should not be discounted. Thus, the causes of PDRM in an ambulatory elderly population have been explored more fully.

The study was also beneficial in working with a managed care organization. The issue of preventable drug-related morbidity was brought to light in the organization and important working relationships were developed. The onus for action rests with the organization to use the data.

The study adds to the measurement options available for quality improvement in the medication use process. We were able to demonstrate that a measure of PDRM can lead to a root cause analysis. The design and implementation of interventions should follow to improve the quality of the medication use system.

Theoretical Contribution

The theoretical contributions are in the areas of measurement and quality improvement. In particular, the validity of explicit definitions has been explored and new doors for research have been opened.

The measurement of patterns of care and corresponding adverse outcomes in an administrative database was an important advancement over published work. This is especially true as it relates to preventable drug-related morbidity in the elderly.

The validity of a measure of preventable drug-related morbidity was approached using a comprehensive framework. The use of Messick's framework for validity offers a credible structure for evidence regarding the interpretation and use of the measure. Additional studies will add to the validation of our measure of PDRM.

The issue of preventability of drug-related events was addressed prospectively using a well-defined framework and a panel of experts. This framework made the

process explicit, rather then relying in expert opinion. This is an important advancement over implicit evaluations.

Finally, the idea of quality assessment and improvement was approached. The measure of PDRM was used by an expert panel to determine if the data could be used to identify the cause of quality problems. The resultant cause-and-effect diagrams demonstrate their possible application to improving the quality of the medication use system.

Contribution to Health Care

Contributions to health care rest in the improvement of patient safety and reducing costs. A new method of defining and measuring the problem of PDRM is put forth as useful. This new measure will help uncover a long hidden problem and improve the quality of the medication use system. The result will be a health care system that is safer for patients and more rewarding for health care practitioners. The financial impact on the health care system could be staggering, saving several billion dollars a year.

Health care in general may also benefit through the new measurement techniques used. This includes the development and use of explicit measure applied to an automated database. Application of a measure by several health care organizations will make benchmarking possible. Benchmarking and applying best practices will help improve the quality of the medication use system.

Health care may also benefit by the use of medical record coders in the standard procedure for operationalizing the definitions. The ability for others to replicate the process adds to reliability in coding. The coding process developed for this study is being replicated in England and Canada.

Contribution to the Profession of Pharmacy

The contribution to the profession of pharmacy can be seen in the call for improved communication and monitoring systems for preventing drug-related injuries. The improvement in communication systems will open up opportunities for pharmacist involvement as a member of the patient care team. If pharmacist involvement in the patient care process increases, job satisfaction and standing will improve.

Future Areas for Study

The results of our study open up a wide array of opportunities for future research. Chief among these will be the use of explicit measures applied to administrative databases. This will be especially true for ambulatory patients. Explicit measures should be made available for study across several managed care organizations.

Indicator development based on the explicit definitions should also be explored. The study provided some initial information about the association between the pattern of care and corresponding outcome. Both the outcome and pattern of care should be studied as indicators. Outcome indicators could signal populations of patients who need disease management interventions. Pattern of care indicators could also be studied on a population basis to determine the quality of the medication use system. However, patterns of care should also be studied as an indicator of potential problems for individual patients.

Each individual definition should be studied to determine additional information that is needed to make it more clinically relevant. One area that is recommended is the amount of time between the pattern of care and the outcome that a clinician could reasonably expect the event to occur. This would help to further define the association between the pattern of care and the outcome, and the PTOV measure for each. This

could be done by inserting a question into the Delphi process asking them for a reasonable time and a range of time for the outcome to occur given the pattern of care.

The validity of the definitions should be further tested with the review of patient charts as a criterion for comparison. Thus, sensitivity and specificity of each definition may be assessed. This would help determine the need for implicit evaluation in further studies.

The validity of the measures should foster future research in the area of labels attached to the measure and the social implications. The issue of the label attached to the measure would help with the consequential basis for interpretation. In this area, the idea of preventability and poor quality should be studied. The social implications of the measure address the consequential basis for the use of a measure. Future studies should address organizations that choose to measure and report preventable drug-related morbidity and the impact on their business. Inclusion as part of a "report card" system may open these organizations up to social pressures to improve the medication use system or risk losing business.

Future studies on risk factors and resource use should be done in large administrative databases. The current study was not able to assess the causality of these components. Resource use is particularly important since preventing these events could save billions of dollars in the health care system.

APPENDIX A
GERIATRIC MEDICINE EXPERT PANEL MEMBERS

Expert panel member	Qualifications
Samir Array, M.D.	Family Medicine Board Certified in Geriatrics Clinical Assistant Professor, Community Health and Family Medicine
James Bomhard, M.D.	Internal Medicine
Robert Curry, M.D.	Family Medicine Professor and Chair, Community Health and Family Medicine
Richard Glock, M.D.	Internal Medicine
Louis Laramoyeux, D.O.	Family Medicine
Harold Reeder, M.D.	Family Medicine Board Certified in Geriatrics Clinical Associate Professor and Program Director, Community Health and Family Medicine
Jeffery Weitzner, M.D.	Internal Medicine

NOTE: All physicians were members of the MCO provider network

APPENDIX B
INITIAL MAILING AND INSTRUCTIONS TO THE DELPHI PANEL

Dear Dr. X

Thank you for agreeing to participate on the Geriatric Medicine Expert Panel for Blue Cross/Blue Shield and the University of Florida. Your expertise will be valuable in looking at medication use from an entirely different perspective.

A major problem in the elderly is preventable drug-related morbidity. Preventability is defined as those outcomes that are recognizable and foreseeable, and where the causality is identifiable and controllable.

The attached survey contains detailed instructions to help you define preventable drug-related morbidity in the elderly. Based on past surveys, it should take between 60-90 minutes to complete. Your input is extremely important. Please return the survey of possible preventable drug-related morbidities, along with any comments, by Friday, December 17, 1999. Approximately 7-10 days after that, you will receive a revised survey based on the comments of all seven participants.

You may fax the survey back to me at (352) 392-7782. Please call me at (352) 392-9035 if you have any questions or email me at; faris@cop3.health.ufl.edu.

Thanks again for participating in this important task.

Sincerely,

Richard J. Faris, M.S., R.Ph.

Survey Instructions

You will be helping to define *preventable drug-related morbidities* in the elderly. First, here are a couple definitions:

(1) *Preventable drug-related morbidity (adverse event, drug misadventure, etc.)* is defined as a clinical outcome in which drug therapy has not produced a reasonable intended result by (a) producing a noxious, unintended and undesired drug effect, or (b) by failing to produce the intended effect within a reasonable time.

(2) *Preventable drug-related morbidity* (a) results from an unacceptable quality of care (e.g., failure to meet consensus guidelines), or (b) occurs after a *drug-related problem*.

(3) *Preventability:* There are four defining characteristics of preventable drug-related morbidity. The *drug-related problem* must be recognizable and the likelihood of a drug-related morbidity must be foreseeable. In addition, the cause(s) of the problem (and subsequent drug-related morbidity) must be identifiable, and those causes must be controllable. *Preventable drug-related morbidity*, therefore, results from unrecognized or unresolved *drug-related problems*.

- A *drug-related problem* might be recognizable and interpretable by the patient in whom the event occurs, a lay caretaker, or a health professional (physician, pharmacist, etc.)

Here are the survey instructions:

- The **objective of this exercise** is to develop criteria for preventable drug-related morbidity using the four defining characteristics. Each of the following examples will describe a *drug-related morbidity* and additional information that may or may not (in your judgement) relate to quality standards or describe a drug-related problem.

- In order to evaluate whether the following examples are types of preventable drug-related morbidities, you should read the **outcomes and patterns of care** and answer the following questions:
    1. *For most older persons, should health professionals (physicians, pharmacists, etc.) be able to **recognize** significant problems in this pattern of care?*
    2. *For most older persons, should the health professional be able to **foresee the possibility of the outcome**, if those problems were not resolved?*
    3. *Should most health professionals see **how to change** the pattern of care to prevent the outcome?*
    4. *Should most health professionals **actually change** the pattern of care?*

    - If you answer "**Yes**" to all four of these questions, then this is a type of preventable drug-related morbidity and you should check the "**Yes**" box.

- If you answer "**No**" to one or more of these questions, then this is **not** a type of preventable drug-related morbidity and you should check the "**No**" box. If you answered "**No**", please specify why. You may wish to describe whether there is some other element that could be added to the pattern of care that would make it a stronger, clearer, or less ambiguous definition of preventable drug-related morbidity. This section is very important to complete. Please be as specific as you possibly can. For example, if you believe the pattern of care should be changes (e.g., a lab value should be monitored every 2 months instead of every 3 months) or something is missing (e.g., a duration of use of a drug should be specified) then please write that in the space provided. Also, if you felt the possible preventable drug-related morbidity did not meet any one of the four criteria, then please state what caused you to answer the way you did (e.g., you feel additional laboratory tests would be needed in order to identify causality).

  If, for some reason, you answer "**Yes**" to all four questions, but you still think you should check the "**No**" box, please describe your reservations or concerns.

- Finally, there is a space at the end of the list for any additional preventable drug-related morbidities in older adults that you feel are important to add. Any additional definitions you could provide based on your knowledge and experience will be a welcomed addition to the panel.

  Thank you again for your time and effort in this endeavor.

APPENDIX C
ROOT CAUSE ANALYSIS EXPERT PANEL

Expert panel member	Qualifications
Birem Amin, Pharm.D.	Family Practice Pharmacist University ambulatory clinic
Stephen J. Clark, M.D.	Family Medicine MCO provider network
George Mayzell, M.D.	Internal Medicine Board Certified in Geriatrics MCO regional medical director
Stuart Millstone, M.D.	Pulmonologist Board Certified in Pulmonology MCO provider network
Mitchell S. Rothstein, M.D.	Pulmonologist Board Certified in Pulmonology MCO provider network
Debra Swartwood, M.S., R.Ph.	MCO Clinical Pharmacy Manager

APPENDIX D
FINAL PREVENTABLE DRUG-RELATED MORBIDITY DEFINITIONS

1. This **outcome** has occurred after the pattern of care below:
   ER visit/hospitalization due to depression and/or increase in dosage of antidepressant

   This is the **pattern of care**:
   1. History/diagnosis of depression
   2. Use of long-acting benzodiazepine (e.g., Librium, Valium, Centrax, Paxipam, Dalmane, Azaene/Tranxene, etc.)

2. This **outcome** has occurred after the pattern of care below:
   Theophylline toxicity

   This is the **pattern of care**:
   1. Use of theophylline
   2. Drug level not done at least every 6 months

3. This **outcome** has occurred after the pattern of care below:
   Bipolar exacerbation and/or ER visit/hospitalization due to bipolar disorder.

   This is the **pattern of care**:
   1. Diagnosis/history of bipolar disorder
   2. Use of lithium
   3. Drug level not done at least every three months

4. This **outcome** has occurred after the pattern of care below:
   Major and/or minor hemorrhagic event

   This is the **pattern of care**:
   1. Use of IV heparin
   2. PTT not done at least every day

5. This **outcome** has occurred after the pattern of care below:
   Gastritis and/or upper GI bleed and/or upper GI perforation and/or GI ulcers and anemia

   This is the **pattern of care**:
   1. History/diagnosis of ulcers and/or GI bleeding
   2. NSAID use for at least 1 month

6. This **outcome** has occurred after the pattern of care below:
   ER visit/hospitalization due to depression and/or an increase in the dosage of antidepressant

   This is the **pattern of care**:
   1. History/diagnosis of depression
   2. Use of a barbiturate (e.g., butalbital)

7. This **outcome** has occurred after the pattern of care below:
   ER visit/hospitalization due to depression and/or increased dosage of antidepressant

   This is the **pattern of care**:
   1. History/diagnosis of depression
   2. Use of a sympatholytic antihypertensive (e.g., reserpine, methyldopa, clonidine, etc.)

8. This **outcome** has occurred after the pattern of care below:
   Status epilepticus and/or ER visit/hospitalization due to seizure activity

   This is the **pattern of care**:
   1. Use of anticonvulsant requiring drug level monitoring (e.g., phenytoin, carbamazepine, valproic acid)
   2. Drug level not done upon initiation of therapy and at least every 6 months thereafter

9. This **outcome** has occurred after the pattern of care below:
   Lithium toxicity

   This is the **pattern of care**:
   1. Use of lithium
   2. Lithium level not done monthly until stable, then every 3 months

10. This **outcome** has occurred after the pattern of care below:
    ER visit/hospitalization due to hyperthyroidism

    This is the **pattern of care**:
    1. Use of thyroid or antithyroid agent (e.g., levothyroxine, propylthiouricil, etc.)
    2. T4/TSH not done within 6 weeks after initiation of therapy and at least every 12 months thereafter

11. This **outcome** has occurred after the pattern of care below:
    ER visit/hospitalization due to a major/minor hemorrhagic event

This is the **pattern of care**:
1. Warfarin use
2. NSAID use (e.g., diclofenac, ibuprofen, ketoprofen, etc.)
3. INR not done within 10 days

12. This **outcome** has occurred after the pattern of care below:
ER visit/hospitalization due to hypothyroidism

This is the **pattern of care**:
1. Lithium use for at least 6 months
2. TSH not done at least every 6 months

13. This **outcome** has occurred after the pattern of care below:
Blood dyscrasias/thrombocytopenia

This is the **pattern of care**:
1. Use of ticlopidine (Ticlid)
2. CBC/platelets not done at baseline, within 2 weeks of start of therapy and within 2 months

14. This **outcome** has occurred after the pattern of care below:
Rebound congestion

This is the **pattern of care**:
1. Use of long-acting nasal spray (e.g., oxymetazoline) for more than 3 days

15. This **outcome** has occurred after the pattern of care below:
Acute urinary retention

This is the **pattern of care**:
1. Diagnosis/history of bladder atony due to diabetes
2. Use of imipramine

16. This **outcome** has occurred after the pattern of care below:
Acute respiratory failure

This is the **pattern of care**:
1. History/diagnosis of severe COPD
2. Use of medium to long-acting benzodiazepines

17. This **outcome** has occurred after the pattern of care below:
Acute urinary retention

This is the **pattern of care**:
1. History/diagnosis of benign prostatic hypertrophy (BPH)
2. Use of an anticholinergic agent

18. This **outcome** has occurred after the pattern of care below:
    ER visit/hospitalization due to liver toxicity

    This is the **pattern of care**:
    1. Use of troglitazone (Rezulin)
    2. Liver function tests not done at baseline and at least monthly for the first 8 months of therapy and at least every 2 months for the remainder of the first year

19. This **outcome** has occurred after the pattern of care below:
    ER visit/hospitalization due to congestive heart failure and/or fluid overload

    This is the **pattern of care**:
    1. History/diagnosis of high blood pressure (over 140/90) and/or congestive heart failure
    2. NSAID use for at least 3 months

20. This **outcome** has occurred after the pattern of care below:
    ER visit/hospitalization for hypokalemia

    This is the **pattern of care**:
    1. Use of potassium-wasting diuretic (e.g., hydrochlorothiazide, etc.)
    2. No concurrent use of potassium supplement
    3. Electrolytes not checked at least every 2 months initially, then every 6 months

21. This **outcome** has occurred after the pattern of care below:
    Anticonvulsant drug toxicity

    This is the **pattern of care**:
    1. Use of an anticonvulsant requiring drug level monitoring (e.g., phenytoin, carbamazepine, valproic acid)
    2. Drug level not done at least every 6 months

22. This **outcome** has occurred after the pattern of care below:
    ER visit/hospitalization due to hypothyroidism

    This is the **pattern of care**:
    1. Use of thyroid or antithyroid agent (e.g., levothyroxine, propylthiouricil, etc.)
    2. T4/TSH not done before therapy starts and at least every 12 months thereafter

23. This **outcome** has occurred after the pattern of care below:
    Hospitalization/ER visit due to worsening renal impairment and/or acute renal failure and or renal insufficiency

This is the **pattern of care**:

1. Diagnosis/history of moderate to severe renal impairment/ history of kidney disease
2. Use of a select urinary antiinfective agent (nalidixic acid, nitrofurantoin or methenamine complexes)
3. BUN/serum creatinine not done within 30 days of initiation of therapy and at least every 6 months

24. This **outcome** has occurred after the pattern of care below:
Aminoglycoside toxicity (acute renal failure and/or renal insufficiency and/or vestibular damage and/or auditory damage)

This is the **pattern of care**:

1. Use of an aminoglycoside
2. Serum creatinine not done before and after therapy (and if therapy longer than 7 days, not done at least every 7 days)
3. At least one drug level not done

25. This **outcome** has occurred after the pattern of care below:
COPD exacerbation and/or ER visit/hospitalization due to COPD

This is the **pattern of care**:

1. Diagnosis/history of COPD
2. Use of a beta-blocker (e.g., propranolol, etc.)

26. This **outcome** has occurred after the pattern of care below:
Hypertension/tachycardia

This is the **pattern of care**:

1. History of hypertension
2. Use of decongestants

27. This **outcome** has occurred after the pattern of care below:
ER visit/hospitalization due to worsening renal impairment and/or acute renal failure and/or renal insufficiency

This is the **pattern of care**:

1. Diagnosis/history of moderate to severe renal impairment and/or history of kidney disease
2. Use of tetracycline
3. BUN/serum creatinine not done within 30 days of initiation of therapy and at least every 6 months

28. This **outcome** has occurred after the pattern of care below:
ER visit/hospitalization due to hyperkalemia

This is the **pattern of care**:
1. Use of ACE inhibitor
2. Electrolytes/CBC not done at least every 6 months

29. This **outcome** has occurred after the pattern of care below:
Blood dyscrasias and/or hyponatremia and/or excessive water retention and/or syndrome of inappropriate antidiuretic hormone (SIADH)

This is the **pattern of care**:
1. Use of carbamazepine
2. Electrolytes/CBC not done before therapy initiated, at least weekly during the first month of therapy, at least monthly during the next 5 months of therapy, and at least every 6 months thereafter

30. This **outcome** has occurred after the pattern of care below:
Acute renal failure and/or renal insufficiency

This is the **pattern of care**:
1. Use of lithium
2. BUN/serum creatinine not done at least every 3 months

31. This **outcome** has occurred after the pattern of care below:
Digoxin toxicity

This is the **pattern of care**:
1. Use of digoxin
2. BUN/serum creatinine not done at least every 6 months
3. Digoxin level not done at least every 6 months

32. This **outcome** has occurred after the pattern of care below:
Gastritis and/or upper GI bleeds and/or GI perforations and/or GI ulcers and anemia

This is the **pattern of care**:
1. History/diagnosis of ulcers and/or gastrointestinal bleeding
2. Use of an oral corticosteroid (e.g., prednisone) for at least 3 months

33. This **outcome** has occurred after the pattern of care below:
ER visit/hospitalization due to congestive heart failure and/or heart block

This is the **pattern of care**:
1. History/diagnosis of congestive heart failure with heart block or advanced bradycardia
2. Use of digoxin

34. This **outcome** has occurred after the pattern of care below:
    Acute renal failure and/or renal insufficiency

    This is the **pattern of care**:
    1. Use of an ACE inhibitor
    2. BUN/serum creatinine not done at initiation of therapy and at least every 3-6 months thereafter

35. This **outcome** has occurred after the pattern of care below:
    Major and/or minor hemorrhagic event

    This is the **pattern of care**:
    1. Use of warfarin
    2. INR not done before therapy starts and at least every month thereafter

36. This **outcome** has occurred after the pattern of care below:
    Secondary myocardial infarction

    This is the **pattern of care**:
    1. History/diagnosis of myocardial infarction
    2. No use of ASA and/or beta blocker (e.g., metoprolol)

37. This **outcome** has occurred after the pattern of care below:
    Blood dyscrasias

    This is the **pattern of care**:
    1. Concurrent use of trimethoprim/sulfamethoxazole (Bactrim/Septra) and methotrexate
    2. WBC/platelets/CBC not done at least every 4 weeks

38. This **outcome** has occurred after the pattern of care below:
    ER visit/hospitalization due to a major/minor hemorrhagic event

    This is the **pattern of care**:
    1. Warfarin use
    2. Antibiotic use (e.g., Bactrim, etc.)
    3. PT not done within 5 days

39. This **outcome** has occurred after the pattern of care below:
    Gastritis and/or upper GI bleed and/or GI perforation and/or GI ulcer and anemia

    This is the **pattern of care**:
    Use of 2 or more NSAIDS concurrently for at least 2 weeks

40. This **outcome** has occurred after the pattern of care below:
    Acute renal failure and/or renal insufficiency

This is the **pattern of care**:
1. Use of allopurinol
2. BUN/serum creatinine not done at least every 6 months

41. This **outcome** has occurred after the pattern of care below:
ER visit/hospitalization due to depression and/or increase in dosage of antidepressant

This is the **pattern of care**:
1. History/diagnosis of depression
2. Use of moderate to high lipophilic beta-adrenergic blocking agent (e.g., propranolol, pindolol, etc.)

42. This **outcome** has occurred after the pattern of care below:
Falls and/or bone fracture and/or bone break

This is the **pattern of care**:
1. Use of muscle relaxants
2. Use of cough codeine-containing cough suppressants

43. This **outcome** has occurred after the pattern of care below:
Patient fall and hip fracture

This is the **pattern of care**:
1. Patient on alpha blocker
2. Standing BP not checked within 2 months of initiation of therapy

44. This **outcome** has occurred after the pattern of care below:
Fall and/or hip fracture and/or other bone fracture and/or bone break

This is the **pattern of care**:
Use of long half-life hypnotic/anxiolytic (e.g., flurazepam, diazepam, chlordiazepoxide, etc.)

45. This **outcome** has occurred after the pattern of care below:
ER visit/hospitalization due to congestive heart failure

This is the **pattern of care**:
1. Diagnosis/history of congestive heart failure
2. Not on an ACE inhibitor (e.g., captopril, enalapril, etc.)

46. This **outcome** has occurred after the pattern of care below:
Acute renal failure and/or renal insufficiency

This is the **pattern of care**:

1. NSAID use for at least 3 months
2. BUN/serum creatinine not done at least every 3 months

47. This **outcome** has occurred after the pattern of care below:
ER visit/hospitalization due to congestive heart failure

This is the **pattern of care**:

1. History/diagnosis of congestive heart failure
2. Use of an antiarrhythmic agent (e.g., disopyramide, procainamide, etc.)

48. This **outcome** has occurred after the pattern of care below:
Asthma exacerbation and/or status asthmaticus and/or ER visit/hospitalization due to asthma

This is the **pattern of care**:

1. Diagnosis of moderate to severe asthma
2. Use of a bronchodilator
3. No use of maintenance corticosteroid (e.g., beclomethasone, etc.)

49. This **outcome** has occurred after the pattern of care below:
Fall and/or hip fracture and/or other bone fracture and/or bone break.

This is the **pattern of care**:

1. Use of tricyclic antidepressant (e.g., amitriptyline, doxepin, imipramine, etc.)

APPENDIX E
MNEMONICS FOR CONSENSUS-APPROVED DEFINITIONS

Definition[a]	Mnemonic	Definition	Mnemonic[a]
1	Dep/Hx-Benzo	26	HTN/Hx-Decon
2	Theo/DrugLvl	27	ARnF/Hx-TCN-BUNCr
3	BP/Hx-Li-DrugLvl	28	HyprK/ACEI-EleCBC
4	Hmr/hep-NoLab	29	Bldys/Cbz-EleCBC
5	GI/Hx-NSAID	30	ARnF/Li-BUNCr
6	Dep/Hx-Barb	31	Dig/Dig-BUNCr-DrugLvl
7	Dep/Hx-Symp	32	GI/Hx-OCort
8	Seiz/Antconv-DrugLvl	33	CHF/Hx-Dig
9	Li/Li-DrugLvl	34	ARnF/ACEI-BUNCr
10	Hyprth/Thy-T4TSH	35	Hmr/War-INR
11	Hmr/War-NSAID-INR	36	MI/Hx-ASA-BB
12	Hypoth/Li-TSH	37	Bldys/TMPSMX-NoLab
13	Bldys/Tic-CBCP	38	Hmr/War-ABx-NoLab
14	RC/Lan	39	GI/NSAID
15	AUR/Hx-Imip	40	ARnF/Allp-BUNCr
16	ARsF/COPD-Benzo	41	Dep/Hx-BB
17	AUR/Hx-Antic	42	FB/MscRelax
18	LvrTox/Rez-LvrTest	43	FB/AB-SBP
19	CHF/Hx-NSAID	44	FB/SedHyp
20	HypoK/Kwd-NoK-Elec	45	CHF/Hx-ACEI
21	Antconv/Anticonv-DrugLvl	46	ARnF/NSAID-BUNCr
22	Hypoth/Thy-T4TSH	47	CHF/Hx-AArhy
23	ARnF/Hx-SUI-BUNCr	48	Asth/Hx-Bdilat-ICort
24	Amgly/Amgly-SCr-DrugLvl	49	FB/TCA
25	COPD/Hx-BB		

[a]Definition number from Appendix D
NOTE: Alphabetical list of mnemonics in Appendix F

APPENDIX F
ALPHABETICAL MNEMONIC LIST

Mnemonic	Outcome or pattern of care
AArhy	antiarrhythmic
AB	Alpha blocker
ABx	Antibiotics
ACEI	ACE Inhibitor
Allp	Allopurinol
Amgly	Aminoglycoside use or toxicity
Antic	Anticholinergic
Anticonv	Anticonvulsant use or toxicity
ARnF	Acute renal failure
ARsF	Acute respiratory failure
ASA	Aspirin
Asth	Asthma
AUR	Acute urinary retention
Barb	Barbiturate
BB	Beta-blocker
Bdilat	Bronchodilator
Benzo	Benzodiazepine
Bldys	Blood dyscrasias
Bp	Bipolar
BUNCr	BUN and serum creatinine
CBCP	CBC and platelets
Cbz	Carbamazepine
CHF	Congestive heart failure
COPD	COPD
Decon	Decongestant
Dep	Depression
Dig	Digoxin use or toxicity
DrugLvl	Drug level
Elec	Electrolytes
EleCBC	Electrolytes and CBC
FB	Fall or bone break
GI	Gastrointestinal
Hep	Heparin
Hmr	Hemorrhage
HTN	Hypertension

Mnemonic	Outcome or pattern of care
Hx	History
HypoK	Hypokalemia
Hypoth	Hypothyroidism
HyprK	Hyperkalemia
Hyprth	Hyperthyroidism
ICort	Inhaled corticosteroid
Imip	Imipramine
INR	INR level
Kwd	Potassium wasting diuretic
Lan	Long-acting nasal spray
Li	Lithium use or toxicity
LvlTox	Liver toxicity
LvrTest	Liver function tests
MI	Myocardial infarction
MscRelax	Muscle relaxants
NoK	No potassium supplement
NoLab	No laboratory monitoring done
NSAID	Non-steroidal anti-inflammatory drug
Ocort	Oral corticosteroids
RC	Rebound congestion
Rez	Rezulin
SBP	Standing blood pressure
SCr	Serum creatinine
SedHyp	Sedative/hypnotic
Seiz	Seizure
SUI	Select urinary antiinfectives
Symp	Sympatholytic antihypertensive
T4TSH	T4/TSH level
TCA	Tricyclic antidepressant
TCN	Tetracycline
Theo	Theophylline toxicity
Thy	Thyroid or antithyroid agent
Tic	Ticlodipine
TMPSMX	Trimethoprim/sulfamethoxazole
TSH	TSH level
War	Warfarin

APPENDIX G
NUMBER OF PATIENTS WITH EACH PDRM DEFINITION

Definition[a]	Mnemonic[b]	Instances of PDRM[c]	Percent of total PDRM[c]
1	Dep/Hx-Benzo	56	4.1%
2	Theo/DrugLvl	0	0.0%
3	BP/Hx-Li-DrugLvl	0	0.0%
4	Hmr/hep-NoLab	0	0.0%
5	GI/Hx-NSAID	63	4.6%
6	Dep/Hx-Barb	1	0.1%
7	Dep/Hx-Symp	35	2.6%
8	Seiz/Antconv-DrugLvl	10	0.7%
9	Li/Li-DrugLvl	0	0.0%
10	Hyprth/Thy-T4TSH	1	0.1%
11	Hmr/War-NSAID-INR	0	0.0%
12	Hypoth/Li-TSH	0	0.0%
13	Bldys/Tic-CBCP	0	0.0%
14	RC/Lan	0	0.0%
15	AUR/Hx-Imip	0	0.0%
16	ARsF/COPD-Benzo	19	1.4%
17	AUR/Hx-Antic	4	0.3%
18	LvrTox/Rez-LvrTest	0	0.0%
19	CHF/Hx-NSAID	80	5.9%
20	HypoK/Kwd-NoK-Elec	44	3.2%
21	Antconv/Anticonv-DrugLvl	0	0.0%
22	Hypoth/Thy-T4TSH	103	7.6%
23	ARnF/Hx-SUI-BUNCr	0	0.0%
24	Amgly/Amgly-SCr-DrugLvl	0	0.0%
25	COPD/Hx-BB	54	4.0%
26	HTN/Hx-Decon	0	0.0%
27	ARnF/Hx-TCN-BUNCr	0	0.0%
28	HyprK/ACEI-EleCBC	14	1.0%
29	Bldys/Cbz-EleCBC	0	0.0%
30	ARnF/Li-BUNCr	0	0.0%
31	Dig/Dig-BUNCr-DrugLvl	1	0.1%
32	GI/Hx-OCort	38	2.8%
33	CHF/Hx-Dig	184	13.5%
34	ARnF/ACEI-BUNCr	1	0.1%

Definition[a]	Mnemonic[b]	Instances of PDRM[c]	Percent of total PDRM[c]
35	Hmr/War-INR	3	0.2%
36	MI/Hx-ASA-BB	54	4.0%
37	Bldys/TMPSMX-NoLab	0	0.0%
38	Hmr/War-ABx-NoLab	0	0.0%
39	GI/NSAID	129	9.5%
40	ARnF/Allp-BUNCr	1	0.1%
41	Dep/Hx-BB	15	1.1%
42	FB/MscRelax	1	0.1%
43	FB/AB-SBP	0	0.0%
44	FB/SedHyp	42	3.1%
45	CHF/Hx-ACEI	270	19.9%
46	ARnF/NSAID-BUNCr	2	0.1%
47	CHF/Hx-AArhy	37	2.7%
48	Asth/Hx-Bdilat-ICort	89	6.5%
49	FB/TCA	8	0.6%

[a]Definition number matches Appendix D
[b]Mnemonics in appendices E and F
[c]PDRM: preventable drug-related morbidity
NOTE: 1,359 instances detected in 966 patients

APPENDIX H
PDRM, PATTERN OF CARE ONLY, AND OUTCOME ONLY

Definition[a]	Mnemonic[b]	PDRM[c]	Pattern only[d]	Outcome only
1	Dep/Hx-Benzo	56	1	382
2	Theo/DrugLvl	0	83	2
3	BP/Hx-Li-DrugLvl	0	0	43
4	Hmr/hep-NoLab	0	0	1571
5	GI/Hx-NSAID	63	1	760
6	Dep/Hx-Barb	1	0	512
7	Dep/Hx-Symp	35	0	426
8	Seiz/Antconv-DrugLvl	10	41	164
9	Li/Li-DrugLvl	0	3	76
10	Hyprth/Thy-T4TSH	1	319	41
11	Hmr/War-NSAID-INR	0	2	1570
12	Hypoth/Li-TSH	0	3	712
13	Bldys/Tic-CBCP	0	6	99
14	RC/Lan	0	0	61
15	AUR/Hx-Imip	0	3	169
16	ARsF/COPD-Benzo	19	173	157
17	AUR/Hx-Antic	4	31	163
18	LvrTox/Rez-LvrTest	0	56	66
19	CHF/Hx-NSAID	80	814	680
20	HypoK/Kwd-NoK-Elec	44	748	318
21	Antconv/Anticonv-DrugLvl	0	71	0
22	Hypoth/Thy-T4TSH	103	175	566
23	ARnF/Hx-SUI-BUNCr	0	0	250
24	Amgly/Amgly-SCr-DrugLvl	0	0	350
25	COPD/Hx-BB	54	1	1038
26	HTN/Hx-Decon	0	1	4237
27	ARnF/Hx-TCN-BUNCr	0	0	250
28	HyprK/ACEI-EleCBC	14	465	335
29	Bldys/Cbz-EleCBC	0	14	440
30	ARnF/Li-BUNCr	0	3	250
31	Dig/Dig-BUNCr-DrugLvl	1	97	80
32	GI/Hx-OCort	38	1	854
33	CHF/Hx-Dig	184	50	653
34	ARnF/ACEI-BUNCr	1	314	248

Definition[a]	Mnemonic[b]	PDRM[c]	Pattern only[d]	Outcome only
35	Hmr/War-INR	3	11	1564
36	MI/Hx-ASA-BB	54	44	63
37	Bldys/TMPSMX-NoLab	0	171	10
38	Hmr/War-ABx-NoLab	0	1	1568
39	GI/NSAID	129	1549	760
40	ARnF/Allp-BUNCr	1	19	249
41	Dep/Hx-BB	15	1	471
42	FB/MscRelax	1	5	562
43	FB/AB-SBP	0	0	175
44	FB/SedHyp	42	878	468
45	CHF/Hx-ACEI	270	299	303
46	ARnF/NSAID-BUNCr	2	491	248
47	CHF/Hx-AArhy	37	27	745
48	Asth/Hx-Bdilat-ICort	89	0	173
49	FB/TCA	8	134	547

[a]Definition number matches Appendix D

[b]Mnemonics in appendices E and F

[c]PDRM: preventable drug-related morbidity

[d]Pattern only is before adjustment in the number of days for actual PDRM events.

APPENDIX I
CUT-OFF DAYS FOR PDRM DEFINITIONS BASED ON METHOD

Definition[a,b]	Mean = 1.65 SD[c]	Linear interpolation[d]	Exponential[e]
1 (Dep/Hx-Benzo)	339.98	338	316.68
5 (GI/Hx-NSAID)	255.75	333	394.75
7 (Dep/Hx-Symp)	279.13	311	302.90
8 (Seiz/Antconv-DrugLvl)	264.73	242	117.43
16 (ARsF/COPD-Benzo)	326.12	318	305.83
19 (CHF/Hx-NSAID)	352.87	368	301.04
20 (HypoK/Kwd-NoK-Elec)	311.77	304	300.05
22 (Hypoth/Thy-T4TSH)	377.40	385	228.93
25 (COPD/Hx-BB)	335.77	376	461.34
28 (HyprK/ACEI-EleCBC)	393.64	372	209.16
32 (GI/Hx-Ocort)	257.34	324	352.93
33 (CHF/Hx-Dig)	352.59	385	299.66
36 (MI/Hx-ASA-BB)	82.04	91	235.34
39 (GI/NSAID)	367.08	376	246.43
41 (Dep/Hx-BB)	317.55	302	299.15
44 (FB/SedHyp)	375.71	364	193.43
45 (CHF/Hx-ACEI)	333.42	374	403.14
47 (CHF/Hx-AArhy)	315.95	327	327.23
48 (Asth/Hx-Bdilat-ICort)	379.57	393	328.33

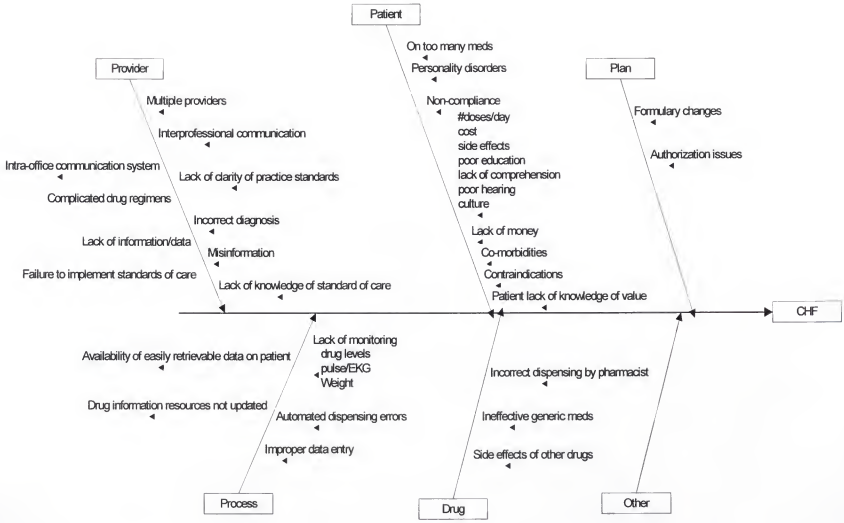
[a]Definition number matches Appendix D
[b]Mnemonic matches appendices E and F
[c]Mean = 1.65 SD: mean plus 1.65 times the standard deviation for each definition
[d]Linear interpolation: linear interpolation of the 95% cut-off value
[e]Exponential: cumulative exponential distribution, 95% cut-off point

APPENDIX J
PATTERN OF CARE ONLY MEASURES BASED ON 95% CUT-OFF VALUE

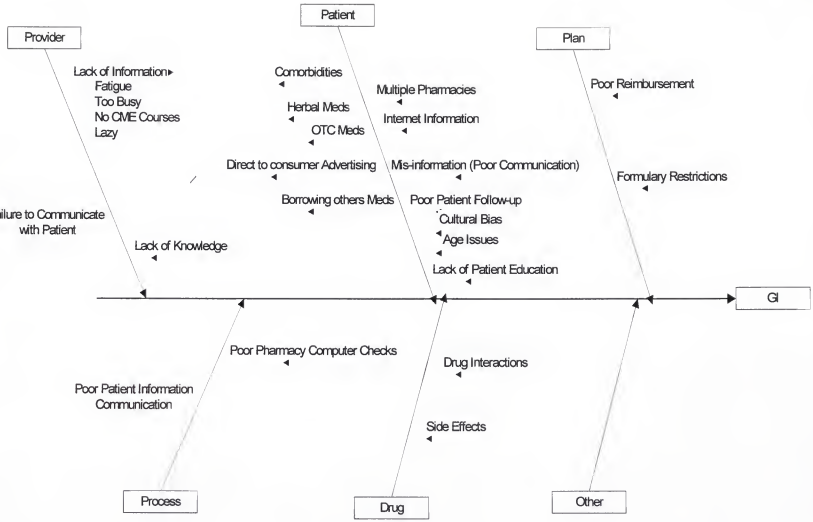
Definition[a,b]	PDRM[c] events	All pattern of care-only patients	Pattern of care patients after 95% cut-off value
1 (Dep/Hx-Benzo)	56	1	0
5 (GI/Hx-NSAID)	63	1	1
7 (Dep/Hx-Symp)	35	0	0
8 (Seiz/Antconv-DrugLvl)	10	41	35
16 (ARsF/COPD-Benzo)	19	173	53
19 (CHF/Hx-NSAID)	80	814	139
20 (HypoK/Kwd-NoK-Elec)	44	748	365
22 (Hypoth/Thy-T4TSH)	103	175	127
25 (COPD/Hx-BB)	54	1	0
28 (HyprK/ACEI-EleCBC)	14	465	360
32 (GI/Hx-Ocort)	38	1	0
33 (CHF/Hx-Dig)	184	50	9
36 (MI/Hx-ASA-BB)	54	44	33
39 (GI/NSAID)	129	1549	929
41 (Dep/Hx-BB)	15	1	0
44 (FB/SedHyp)	42	878	655
45 (CHF/Hx-ACEI)	270	299	90
47 (CHF/Hx-AArhy)	37	27	6
48 (Asth/Hx-Bdilat-ICort)	89	0	0

[a]Definition number matches Appendix D
[b]Mnemonic matches appendices E and F
[c]PDRM: preventable drug-related morbidity

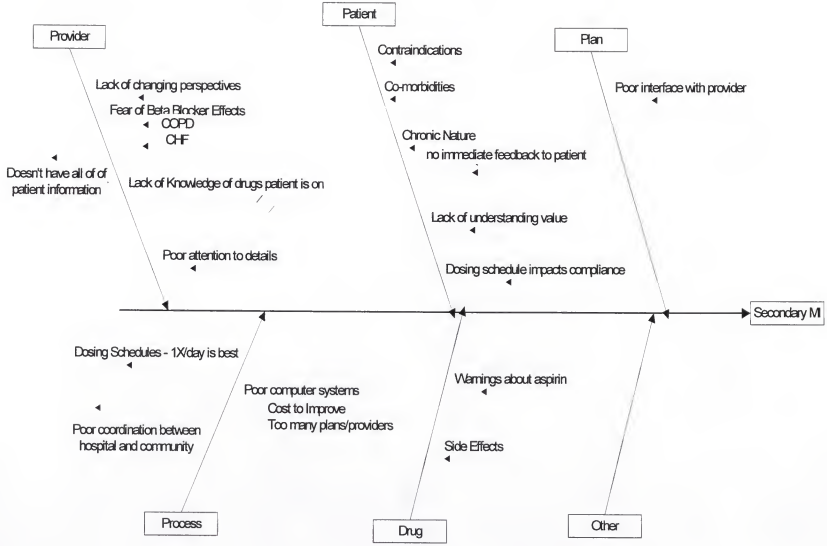
APPENDIX K
CONGESTIVE HEART FAILURE CAUSE-AND-EFFECT DIAGRAM


Patient
Provider
Plan
On too many meds
Personality disorders
Multiple providers
Non-compliance
#doses/day
cost
side effects
poor education
lack of comprehension
poor hearing
culture
Formulary changes
Interprofessional communication
Authorization issues
Intra-office communication system
Lack of clarity of practice standards
Complicated drug regimens
Incorrect diagnosis
Lack of money
Lack of information/data
Misinformation
Co-morbidities
Failure to implement standards of care
Contraindications
Lack of knowledge of standard of care
Patient lack of knowledge of value
CHF
Availability of easily retrievable data on patient
Lack of monitoring
drug levels
pulse/EKG
Weight
Incorrect dispensing by pharmacist
Drug information resources not updated
Automated dispensing errors
Ineffective generic meds
Improper data entry
Side effects of other drugs
Process
Drug
Other

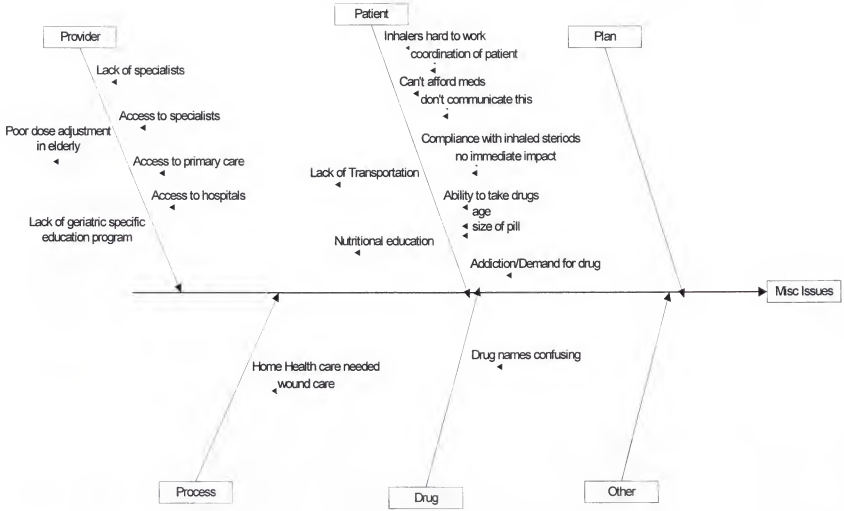
APPENDIX L
GASTROINTESTINAL CAUSE-AND-EFFECT DIAGRAM


Provider
Patient
Plan
Lack of Information
Fatigue
Too Busy
No CME Courses
Lazy
Comorbidities
Multiple Pharmacies
Herbal Meds
Internet Information
OTC Meds
Direct to consumer Advertising
Mis-information (Poor Communication)
Poor Reimbursement
Formulary Restrictions
Borrowing others Meds
Poor Patient Follow-up
Cultural Bias
Age Issues
Failure to Communicate with Patient
Lack of Knowledge
Lack of Patient Education
GI
Poor Pharmacy Computer Checks
Drug Interactions
Poor Patient Information Communication
Side Effects
Process
Drug
Other

APPENDIX M
MYOCARDIAL INFARCTION CAUSE-AND-EFFECT DIAGRAM


Patient
Provider
Plan
Contraindications
Co-morbidities
Poor interface with provider
Lack of changing perspectives
Fear of Beta Blocker Effects
COPD
CHF
Chronic Nature
no immediate feedback to patient
Doesn't have all of of patient information
Lack of Knowledge of drugs patient is on
Lack of understanding value
Poor attention to details
Dosing schedule impacts compliance
Secondary M
Dosing Schedules - 1X/day is best
Warnings about aspirin
Poor computer systems
Cost to Improve
Too many plans/providers
Poor coordination between hospital and community
Side Effects
Process
Drug
Other

APPENDIX N
MISCELLANEOUS CAUSE-AND-EFFECT DIAGRAM


Provider
Patient
Plan
Lack of specialists
Access to specialists
Poor dose adjustment in elderly
Access to primary care
Access to hospitals
Lack of geriatric specific education program
Inhalers hard to work
coordination of patient
Can't afford meds
don't communicate this
Compliance with inhaled steriods
no immediate impact
Lack of Transportation
Ability to take drugs
age
size of pill
Nutritional education
Addiction/Demand for drug
Misc Issues
Home Health care needed
wound care
Drug names confusing
Process
Drug
Other

APPENDIX O
CONSULTANT ANALYSIS OF ROOT CAUSE ANALYSIS

Reaching Consensus on Quality Indicators: A Meeting with Blue Cross/Blue Shield Providers

Introduction

On Thursday, August 31, 2000 three physicians and one pharmacist provider met with three *(managed care organization)* employees and the research team to review a set of quality indicators. The meeting took place in a *(managed care organization)* conference room. The purpose of the meeting was to reach consensus on the root causes of problems inferred by the indicators.

The following report was prepared to provide an overview of the meeting's process. That is, how did the participants appear to react to the to the questions posed and was consensus reached on root causes. A brief description of each provider participant is provided. This is followed by a description of the meeting process. The final section of this report provides some general comments and suggestions.

The Participants

Stephen Clark:

Dr. Clark practices family medicine in Jacksonville, Florida. He arrived wearing a suit, but took off the jacket after greeting the rest of the group. Dr. Clark appeared to be engaged in the process throughout the meeting. He had no problem in responding when asked, and he seemed to jump in when he felt that he had a contribution. While he occasionally prefaced his remarks with the word "gently" (in deference to the *(managed care organization)* participants), he was confident in his remarks. Dr. Clark seemed to have an interest in the bottom line. That is, several of his remarks were prefaced by a comment about what *(the managed care organization)* wanted or how the item under discussion might affect *(the managed care organization's)* bottom line. This may indicate that his comments were directed at that endpoint, not necessarily at how the indicators might help his individual practice.

Mitchell Rothstein:

Dr. Rothstein practices pulmonary and critical care medicine in Orange Park, Florida. He arrived wearing a long sleeve shirt and dress slacks, but no tie. Dr. Rothstein

appeared to be very actively engaged in the meeting process at the onset. In the beginning he was observed to be studying the handouts and taking notes. He asked for clarification of terms and appeared to process the responses. Like Dr. Clark, Dr. Rothstein seemed to have a ready answer when asked. In turn, he would ask for clarification when he needed it. Towards the end of the meeting while he did still participate, his attention seemed to waiver, and at the end of the meeting he left his handouts on the table.

Stuart Millstone:

Dr. Millstone practices pulmonary, internal, and critical care medicine in Orange Park, Florida. It appears that Dr. Rothstein is his partner. He arrived thirty minutes late wearing a long sleeved shirt and dress slacks. While he did arrive after the initial handout of material, he did arrive in time to hear the explanation of how the root cause discussion would take place. While Dr. Millstone did participate when asked he appeared to be the least engaged of the three physicians. On at least two times he engaged Drs. Rothstein and Mayzell in side conversations. He did not sit up to the table, his arms were frequently crossed, and he was observed tapping his fingers on his chair frequently. At one point he left the room after receiving a page.

Birem Amin:

Dr. Amin is a Family Practice Pharmacist at Shands Jacksonville. Dr. Amin also arrived wearing a long sleeved shirt and dress slacks. Of all of the participants Dr. Amin had the least to say. He was observed to make only six comments throughout the meeting. Most of those comments were made only because he was directly asked a question. The lack of participation may be due to a perceived lack of "rank" in the room. That is, the other participants were physicians, employees of the host organization, or part of a research team.

The Meeting Process

Introduction:

The meeting began at 5:30 with some informal introductions and the offer of sandwiches and drinks. After a formal introduction of all in the room, Dr. Mayzell briefly introduced the project and turned the floor over to Richard Faris. *(Mr. Faris)* made a brief presentation and handed out the material to be used during discussion. There was some discussion of the method used for obtaining the indicator results, and time allowed for "studying" the handouts.

Root Causes:

At 6:10 the meeting was turned over to Jill Sanborne, an employee of *(the managed care organization)*. Jill's role was to facilitate this portion of the meeting. She was to direct the discussion to finding the root causes of indicator problems using the

fishbone technique. Jill began the discussion with a question for the participants. This first question was greeted with silence. The participants did not seem to understand the goal of the process/questions. Dr. Mayzell attempted to help, and while there was a brief discussion among the participants, there was not a clear understanding of the process that they were embarking upon.

Ms. Sanborne moved forward and attempted to describe the specific process that they (the participants) would follow for the remainder of the meeting. Again there seemed to be a lack of understanding among the participants. Specifically, Ms. Sanborne asked the participants to think in broad terms (i.e., population) when responding. This seemed to confuse the participants. Also, there was no clear presentation or understanding of how to use the fishbone.

Sensing this lack of understanding both Dr. Hepler and Dr. Mayzell attempted to make the process more concrete. However, it was not until a specific group of indicators (those for CHF) was chosen that the participants began to respond. For one round of responses the participants followed one another as the process would indicate, but after that one round the participants jumped in whenever they had a thought/idea.

While the fishbone diagram was available (as an overhead transparency) and used, it did not seem that the participants fully understood how the available categories and outcome worked together. In fact, at some points *(Mr. Faris)* was placing responses on categories without participant input.

Closing:

There was a definite focus (throughout the time) on ending the meeting as scheduled. At the conclusion of the meeting the participants left quickly without much socializing.

Reflections

Root Causes:

Two questions were raised during this portion of the meeting: 1) is there any utility for you (i.e., the participant) in this data? and 2) did the participants come to consensus on the root causes associated with the indicators? Only Drs. Rothstein and Clark responded immediately and not in the affirmative to question one. There was a small discussion of how to make the information useful, but I did not sense that the participants would dig in and use the information provided by the indicators. Comments made about the reports received from other organizations (e.g., PCS) seem to support a lack of interest in another report.

The question of reaching consensus is harder to directly answer. While there was a good deal of discussion and response to the indicators presented, I do not believe that a general consensus on root causes was reached. There did seem to be consensus and a good number of responses on some specific root causes for specific indicators. However, the participants seemed to have a difficult time thinking in terms of a population. But is this really surprising given their training to focus on the problem(s) presented by an

individual patient? Their task is to solve a very specific problem for the individual in front of them, not the population of Duval County. Comparing the responses to individual indicators may begin to show patterns of root causes, but I would suggest that these be confirmed by the participants or others like them.

In regards to the root causes discussion process, I have some suggestions. First, do not use an overhead transparency for the fishbone diagram. The machine is distracting and dim lights may impede discussion. Second, given the same participant group, I would begin the process with a specific indicator. Use the specific as an example and then move to the general population based questions. Also, be careful of making decisions for the participants (e.g., placing the responses in categories).

In General:

The participant group seemed to be a good match. The pharmacist was the only individual to provide very little input. None of the physician participants seemed to be intimidated by the others and all had no problem in "arguing" their point and suggesting that physicians are at the root of some of the problems. However, at least one participant (Dr. Clark) did seem to focus some of his responses on what would be best for *(the managed care organization)*, not for his own practice. Also, some of the joking (who will have lunch with who) between *(the managed care organization)* personnel and the participants seemed to indicate that the participants understood who had the "power" in the room. That is, *(the managed care organization)* (who may be a major payer in their practice) asked them to participate in a meeting to be held in their conference room with their personnel present. While I understand that *(the managed care organization)* is a sponsor of the research, holding the meeting at a neutral location without *(the managed care organization)* personnel present might alleviate any response bias. Also, physicians are strong, take charge individuals to deal with. Perhaps, a physician facilitator would be better suited to the challenge of keeping them in the process at hand.

In closing, the process seemed to provide some valuable information, the comments, reflections and suggestions made above are meant to enrich the research.

APPENDIX P
MACKINNON'S TOP 12 DEFINITIONS

Preventable drug-related morbidity	MacKinnon events detected	Faris events detected
Outcome: Secondary myocardial infarction **Pattern of Care:** 1. History/diagnosis of myocardial infarction 2. No use of ASA and/or beta blocker (e.g., metoprolol)	24 (15.1%)	54 (4.0%)
Outcome: ER visit/hospitalization due to hyperglycemia **Pattern of Care:** 1. Use of an oral hypoglycemic agent (e.g., chlorpropamide, etc.) 2. Hemoglobin A1c level not done at least every 6 months	18 (11.4%)	N/A[a]
Outcome: ER visit/hospitalization due to hypothyroidism **Pattern of Care:** 1. Use of thyroid or antithyroid agent (e.g., levothyroxine, propylthiouricil, etc.) 2. T4/TSH not done before therapy starts and at least every 12 months thereafter	12 (7.6%)	103 (7.6%)
Outcome: ER visit/hospitalization due to hypoglycemia or hyperglycemia **Pattern of Care:** 1. Use of insulin 2. Hemoglobin A1c level not done at least every 6 months	10 (6.3%)	N/A[a]
Outcome: Acute renal failure and/or renal insufficiency **Pattern of Care:** 1. Use of an ACE inhibitor 2. BUN/serum creatinine not done at initiation of therapy and at least every 3 months thereafter	10 (6.3%)	1 (0.1%)

Preventable drug-related morbidity	MacKinnon events detected	Faris events detected
Outcome: Gastritis and/or upper GI bleed and/or GI perforation and/or GI ulcer and anemia **Pattern of Care:** 1. NSAID use for at least 1 month 2. No concurrent use of a cytoprotective agent (misoprostol) 3. Hemoglobin/hematocrit/CBC not done within 30 days of the start of therapy or not done at least every three months thereafter	8 (5.1%)	N/A[a]
Outcome: ER visit/hospitalization due to congestive heart failure and/or fluid overload **Pattern of Care:** 1. History/diagnosis of high blood pressure (over 140/90) and/or congestive heart failure 2. NSAID use for at least 3 months	8 (5.1%)	80 (5.9%)
Outcome: Acute urinary retention **Pattern of Care:** 1. History/diagnosis of benign prostatic hypertrophy (BPH) 2. Use of an anticholinergic agent	7 (4.4%)	4 (0.3%)
Outcome: ER visit/hospitalization due to extreme hypoglycemia **Pattern of Care:** 1. History/diagnosis of diabetes 2. Use of beta-adrenergic blocking agent (e.g., propranolol, nadolol, etc.)	6 (3.8%)	N/A[a]
Outcome: ER visit/hospitalization due to congestive heart failure **Pattern of Care:** 1. Diagnosis/history of congestive heart failure 2. Not on an ACE inhibitor (e.g., captopril, enalapril, etc.)	6 (3.8%)	270 (19.9%)

Preventable drug-related morbidity	MacKinnon events detected	Faris events detected
Outcome: Aminoglycoside toxicity (acute renal failure and/or renal insufficiency and/or vestibular damage and/or auditory damage) **Pattern of Care:** 1. Use of an aminoglycoside 2. Serum creatinine not done before and after therapy (and if therapy longer than 7 days, not done at least every 7 days) 3. At least one drug level not done	6 (3.8%)	0 (0.0%)
Outcome: Acute renal failure and/or renal insufficiency **Pattern of Care:** 1. NSAID use for at least 3 months 2. BUN/serum creatinine not done at least every 3 months	6 (3.8%)	2 (0.2%)

[a]N/A: specific definition was not measured in Faris' population
NOTE: MacKinnon events from MacKinnon (1999)

APPENDIX Q
FARIS' TOP 10 DEFINITIONS

Preventable drug-related morbidity	Faris events detected	MacKinnon events detected
Outcome: ER visit/hospitalization due to congestive heart failure **Pattern of Care:** 1. Diagnosis/history of congestive heart failure 2. Not on an ACE inhibitor (e.g., captopril, enalapril, etc.)	270 (19.9%)	6 (3.8%)
Outcome: ER visit/hospitalization due to congestive heart failure and/or heart block **Pattern of Care:** 1. History/diagnosis of congestive heart failure with heart block or advanced bradycardia 2. Use of digoxin	184 (13.5%)	4 (2.5%)
Outcome: Gastritis and/or upper GI bleed and/or GI perforation and/or GI ulcer and anemia **Pattern of Care:** Use of 2 or more NSAIDS concurrently for at least 2 weeks	129 (9.5%)	3 (1.9%)
Outcome: ER visit/hospitalization due to hypothyroidism **Pattern of Care:** 1. Use of thyroid or antithyroid agent (e.g., levothyroxine, propylthiouricil, etc.) 2. T4/TSH not done before therapy starts and at least every 12 months thereafter	103 (7.6%)	12 (7.6%)
Outcome: Asthma exacerbation and/or status asthmaticus and/or ER visit/hospitalization due to asthma **Pattern of Care:** 1. Diagnosis of moderate to severe asthma 2. Use of a bronchodilator 3. No use of maintenance corticosteroid	89 (6.5%)	0 (0.0%)

Preventable drug-related morbidity	Faris events detected	MacKinnon events detected
Outcome: ER visit/hospitalization due to congestive heart failure and/or fluid overload **Pattern of Care:** 1. History/diagnosis of high blood pressure (over 140/90) and/or congestive heart failure 2. NSAID use for at least 3 months	80 (5.9%)	8 (5.1%)
Outcome: Gastritis and/or upper GI bleed and/or upper GI perforation and/or GI ulcers and anemia **Pattern of Care:** 1. History/diagnosis of ulcers and/or GI bleeding 2. NSAID use for at least 1 month	63 (4.6%)	2 (1.3%)
Outcome: ER visit/hospitalization due to depression and/or increase in dosage of antidepressant. **Pattern of Care:** 1. History/diagnosis of depression 2. Use of long-acting benzodiazepine (e.g., Librium, Valium, Azaene/Tranxene, etc.)	56 (4.1%)	0 (0.0%)
Outcome: Secondary myocardial infarction **Pattern of Care:** 1. Diagnosis/history of myocardial infarction 2. No use of ASA and/or beta blocker	54 (4.0%)	24 (15.1%)
Outcome: COPD exacerbation and/or ER visit/hospitalization due to COPD **Pattern of Care:** 1. Diagnosis/history of COPD 2. Use of a beta-blocker (e.g., propranolol, etc.)	54 (4.0%)	2 (1.3%)

NOTE: MacKinnon events from MacKinnon (1999)

APPENDIX R
PROCESS-TO-OUTCOME VALUE AFTER ADJUSTMENT FOR NDPO

Definition[a]	Number of PDRMs[b]	Pattern of care-only	Outcome only	Process-to-outcome value
48	89	0	173	1.000
1	56	0	382	1.000
25	54	0	1038	1.000
32	38	0	854	1.000
7	35	0	426	1.000
41	15	0	471	1.000
5	63	1	760	.9844
33	184	9	653	.9534
47	37	6	745	.8605
45	270	90	303	.7500
36	54	33	63	.6207
22	103	127	566	.4478
19	80	139	680	.3653
16	19	53	157	.2639
8	10	35	164	.2222
39	129	929	760	.1219
20	44	365	318	.1076
44	42	655	468	.0603
28	14	360	335	.0374

[a]Definition number matches Appendix D
[b]PDRM: preventable drug-related morbidity
NOTE: NDPO is the Number of Days between the Pattern of care and Outcome

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BIOGRAPHICAL SKETCH

Richard Joseph Faris graduated from Goodrich Senior High School in Fond du Lac, Wisconsin, in 1983. He then attended the University of Mississippi where he received his Bachelor of Science degree in Pharmacy in 1988. In 1988, Dr. Faris began a two-year residency/master's program with United and Children's Hospital and the University of Minnesota. He completed both in the summer of 1990. In July of 1990, Dr. Faris took a position as administrative resident with Shands Hospital at the University of Florida. Dr. Faris began his career in hospital pharmacy administration at Methodist Health Systems in Memphis, Tennessee, in 1991. As the Associate Director of Pharmacy Operations, Dr. Faris was responsible for 100 full time equivalents (FTEs) of pharmacists and technicians, and was instrumental in expanding the pharmaceutical care services provided to all patients in the hospital. In the summer of 1996, Dr. Faris was accepted into the PhD program at the University of Florida. During his education at the University of Florida, Dr. Faris was awarded the American Foundation for Pharmaceutical Education (AFPE) Fellowship for three years. He completed his doctorate degree in Pharmacy Health Care Administration in the summer of 2001. Dr. Faris is currently the Director, Center for Pharmaceutical Outcomes and Policy Research with Johns Hopkins Hospital in Baltimore, Maryland.

I certify that I have read this study and that in my opinion it conforms to acceptable standards of scholarly presentation and is fully adequate, in scope and quality, as a dissertation for the degree of Doctor of Philosophy.

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